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*Gray, A. L.: Southern Med. J., 43:320, April, 1950.

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The Common Cold—Fact and Fancy

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SUMMARY

A great deal of folklore, superstition and emotional reaction is attached to the common cold, but established objective information is quite limited. The evidence concerning etiology, epidemiology, physiology, prevention and treatment of the common cold is briefly summarized and critically evaluated. There is disappointing lack of real progress in any of these aspects of the common cold problem.

THE common cold is probably the commonest human ailment. It is responsible for twice as many of the infant illnesses as any other cause.[8] At least 15 per cent of all time lost by industrial workers has been attributed to colds and although the economic implications have probably been overstated, the total amount of discomfort and reduction of working efficiency caused by this "minor" illness must be enormous.[15]

Most people have a cold two or three times every year. It is usually a mild disease, killing no one, and nowadays the incidence of severe complications is low. However, everyone who has a cold exhibits poignant resentment of the illness, not infrequently transferring this feeling to the person from whom he might have "caught it," and who is consequently made responsible. When afflicted with a cold everyone feels that "medical science ought to do something about it"; he tends to believe that "there must be some good remedy," and easily falls prey to the gaudy advertisements of "sure cures" that fill the scientific journals, magazines, newspapers and comic strips. Almost every new variety of drug to reach the market is given a trial against colds, to be praised at first but soon discarded. And the common cold with its misery and its nuisance continues as before.

Not only is the popular interest in this malady considerable but each individual feels he "knows all about it" and is eager to transmit his knowledge to other sufferers. As a result there are about as many versions of the etiologic delineation, pathogenesis and treatment of the common cold as there are people who have the illness. Scientifically trained physicians tend to laugh at this "vox populi" and discredit its significance. However, it might be well to keep in mind that folklore is made up essentially of observations over centuries and conclusions drawn from them. Erroneous though the *interpretations* may be, repeated and consistent observations on the natural history of the common cold are likely to have some validity. In order to be fully acceptable, the experimental results should agree with, and explain, the observations made every day by physicians and lay people alike.

What is a common cold? From the specific names given to it in various languages (headcold, Schnupfen, rhume de cerveau, etc.) one might expect a well defined clinical entity. Inquiry into the minor upper respiratory infections suffered by different people soon reveals, however, that concepts of what constitutes a common cold vary widely from person to person. For one a "headcold" is mainly coryza with little systemic involvement, for another a feeling of "stuffiness in the head" with prostration, while a third visualizes sore throat, laryngitis and tracheitis. For the purpose of this discussion the "common cold" will be considered to include the entire spectrum of acute minor upper respiratory affections from minimal rhinitis to tracheobronchitis, excluding pneumonitis and influenza. Common symptoms include malaise, headache, roughness or soreness of throat, and nasal discharge

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which is serous at first, purulent later. The symptoms may be fleeting or may last more than a week.

What causes a cold? For centuries it has been well accepted that draughts, sudden changes in temperature, wet feet, dietary indiscretions, emotional upsets, etc., may precipitate an attack of the common cold. More frequently, however, a cold is thought to be "caught" from another person.

Several virus infections with fairly well defined clinical manifestations may give rise to a mild illness indistinguishable from the common cold.[1] This is certainly true of the influenza viruses and probably of the virus responsible for primary atypical pneumonia. However, it seems fairly certain on epidemiological grounds that these viruses are not responsible for a sizable fraction of the common colds ordinarily encountered.

The possibility that the common cold may be a distinct infectious entity has been tested experimentally many times since the original transmission studies of Kruse in 1914.[1, 9, 11, 20, 21, 24, 27, 31] It has usually been found that bacteria-free nasal washings from patients in the early stages of a cold when instilled or sprayed into the noses of healthy human volunteers are capable of inducing colds in 50 to 90 per cent of cases. Such transmissions can be carried out in series from person to person, with washings taken prior to the onset of symptoms. They leave no doubt that a transmissible agent is often present in the common cold and that it can induce the typical symptom complex.

The nature of this agent or agents has not been completely established, but in many ways it has the characteristics of a virus. (Bacteria have been excluded as an important initial etiologic factor.) While a number of investigators have claimed propagation of "cold" viruses in tissue culture or in fertile hens' eggs[12, 19, 24, 26, 31] the evidence to date is not conclusive. However, a good deal has been learned about the behavior of such infectious agents: Their stability on storage at low temperatures[2, 26] their approximate size (20-50 millimicrons),[2] their presence in the nasal secretion at various times, and the duration of the immunity of human volunteers to reinfection after an experimentally induced disease.[2, 9, 25] The failure to adapt any of the agents to ordinary laboratory animals has greatly impeded progress in this direction.

Other support for the "catching," transmissible nature of at least some colds comes from experiences in isolated communities. In Spitzbergen, for example, colds almost vanish from the communities during the winter months of isolation. With the coming of the first ship, an epidemic of colds breaks out, involving most of the population.[23] There are many examples of isolated parties of Arctic explorers who remain free from colds during the rigors of their solitary travels, only to contract colds as soon as they return to civilization.[2] Similarly it is a common experience that people return fit and well from a summer holiday—and promptly come down with a cold as they rejoin their working group.

Thus there seems little doubt that infectious agents, probably of virus nature, are involved at least in some colds. However, the epidemiological features of infectious disease of this type are very complex. They raise the questions of latency of the "cold" agents; of a carrier stage; of the multiplicity of types—or strains—of "cold" viruses and the cross-immunity between such viruses; of the magnitude of an infectious dose; of the relative ease of transmitting infection by sneezes, handkerchiefs, or hands, versus floating airborne particles, and many others. The very complexity of the situation and the inconstant epidemiological pattern strongly suggest that the infectious agent is only a part of the etiologic delineation of the common cold. The other part must be supplied by some host factor, termed "resistance."

This resistance might be a function of vascular responsiveness, of specific immunity, of many nonspecific and unknown factors that keep a person well, such as nutrition, hydration, rest, constitution,[30] etc. It is often assumed that environmental factors (chilling, heating, moisture, dryness, irritants, draughts, etc.) cause colds by lowering the systemic or local resistance. This might permit a latent virus to become active, or might result in more fertile ground for a newly introduced agent.

Can nonspecific environmental factors, or alterations of host response alone, cause colds without the presence of an infectious agent? There can be no question that peripheral chilling results in reflex vasoconstriction in the nasal mucous membranes, or that direct irritation of the mucosa produces disturbances of vascular tone and of mucous film.[18, 28] It is equally established that an allergic reaction, or sometimes a strong emotional upset results in a pattern of response in the upper respiratory tract indistinguishable clinically from the common cold. This consideration forces the conclusion that no certain etiological diagnosis could be made from the clinical picture of an early common cold.

The upper respiratory tract, particularly its mucous membrane, is capable of only a very limited number of responses. These responses may be set in motion by a variety of stimuli. Following the early response of mucous membranes and blood vessels (vasoconstriction, ischemia, vasodilatation, epithelial injury, increased capillary permeability, serous exudation, etc.) the subsequent course (particularly epithelial necrosis, secondary bacterial invasion) may be identical no matter what the original cause of the disturbance. Consequently one must accept the possibility that the environmental factors previously mentioned may produce the picture of a sporadic cold occasionally in the absence of an infectious agent. The limited experimental evidence[2] obtained under controlled conditions has not supported (to date) the theory that chilling, wet feet, or draughts, may cause colds. The importance of reaction of allergic type is well recognized in the terms "perennial" rhinitis, "allergic" rhinitis, etc. These manifestations are indistinguishable from the common cold in all respects except for their greater

frequency of occurrence (more than three or four times a year). Similarly, exaggerated vascular reactions are recognized in "vasomotor" rhinitis.

The recognition of the great similarity of these reactions to the usual common cold inevitably leads to a consideration of the role of histamine in the latter condition. Objective measurements[32] revealed wide variations in the concentration of a histamine-like substance in nasal secretions in cases of common cold and allergic rhinitis alike.

Gordon[16] demonstrated that dilute solutions of histamine phosphate sprayed into the nasal mucosa resulted in sneezing, blanching, edema and increased nasal secretions followed 30 minutes later by pronounced redness of the mucosa. The entire reaction subsided within one hour.

These findings merely emphasize the uniformity of organ response to a variety of stimuli, but do not prove that all "cold"-like responses are necessarily on an allergic or vasomotor basis. A great deal more information is needed before any clear-cut relationship between the common cold and histamine-like substances can be postulated. The widespread use of antihistaminics has contributed little to the understanding of the role of histamine in colds.

Can one prevent a cold? Many infectious diseases induce permanent immunity with a single attack. Others can be prevented by avoiding exposure or by suitable immunization of susceptible persons. None of these features appears to be true of the common cold. Withdrawal into relative isolation may well prevent colds, but return to group-life usually results in a new wave of colds. It is well established that the many "bacterial vaccines" are of no prophylactic value[14] and to date no adequate information on "virus vaccines" is available.

On the assumption that histamine is somehow involved as an etiologic factor in the common cold, antihistaminic drugs have been widely advertised and used on a large scale for prophylactic purposes. In spite of the large volume of antihistaminic drugs sold for this purpose, only a single controlled study has been published.[3] In this study thonzylamine hydrochloride (Neohetramine®) was administered in doses of 50 to 150 mg. daily to 300 persons for a period of six months, while 300 others received a placebo. All persons had "equal chances of exposure to the common cold by intermingling freely."[3] Among the controls only 20 per cent remained free from any colds during the observation period, while among the persons receiving antihistaminic drug, 80 per cent remained well. The results of this prophylactic experiment are statistically significant, but there is great need for verification. Allergists treating many patients with antihistaminic drugs for various disorders over long periods report that in such persons colds develop "with the same frequency and of the same duration as without the drugs."[10] If it is remembered that most persons have only two or three colds per year, serious question arises as to the advisability of taking day in and day out an antihistaminic drug, the chronic side-actions of which are still largely unknown, and which certainly could at best give only partial protection. For persons who have three, four or more colds a year, where the presumptive diagnosis of "vasomotor rhinitis" or "allergic rhinitis" may be justified, the continued administration of antihistaminic agents might be more seriously considered.

Can one effectively treat the "common cold"? The status of therapy for the common cold up to 1946 has been adequately reviewed by Reimann:[29] Bed rest, forced fluids (alcoholic or otherwise) and salicylates tend to make the patient more comfortable, although there is doubt whether these measures in any way influence the severity or duration of the illness. Chemotherapy is indicated for bacterial complications, but not for the basic disorder.

Claims for the effectiveness of antihistaminic drugs in "stopping," "curing" or "killing" the common cold have flooded every physician's mailbox. The approval by the Food and Drug Administration of three such drugs for over-the-counter sale has greatly stimulated the advertising pressure of an industry whose sales are estimated to top $100,000,000 this year.[13] A critical review and evaluation of the published claims for antihistaminic drug therapy in the common cold has been published by the Council on Pharmacy and Chemistry of the American Medical Association.[10] Of several published studies the work of only two groups of investigators could be included; the others employed no controls whatever. The studies of Brewster[5, 6] and of Arminio and Sweet[3] were analyzed in detail. Brewster's earliest studies were quite inadequately controlled. In his later work the statistics were weighted by the inclusion of a high proportion of "cures" in persons manifesting symptoms for less than six hours. Such symptoms have a great tendency to regress spontaneously. Brewster's most significant figures are probably those shown in Table 1.[6]

Even though the difference is statistically significant one cannot but wonder at the results of a study in which 53 per cent of the control group had results the same as those attributed to drug action in

TABLE 1

Duration of symptoms	Treated Group: Number of Patients	Helped: Cured	Helped: Improved	Not Helped	Control Group (Given Placebos): Number of Patients	Helped: Cured	Helped: Improved	Not Helped
12 hours or less	694	322	201	171	140	39	35	66
		46%	29%	25%		28%	25%	47%
		75%				53%		

the treated group. The study of Arminio and Sweet[3] also presented statistically significant data on the shortening of illness by the use of an antihistaminic drug. However, a number of features in their report cast doubt on the validity of their entire study, as has been discussed elsewhere.[10]

A critical appraisal of the results of any experimental work dealing with the common cold is fraught with great difficulties for a number of obvious reasons: (1) There is no universally accepted, clear-cut definition of the disease. (2) There is no clear-cut acceptable relationship between subjective symptoms and objective findings.[22] (3) No clinical or laboratory criteria are available to prove the diagnosis unequivocally in all cases. (4) The variability of the clinical syndrome is great. (5) The etiologic delineation of the common cold is not established. (6) It is quite possible that the common cold syndrome may follow a multitude of etiologic factors.

For these reasons it is doubtful whether the criteria for a completely objective study, as outlined by the council,[10] can ever be fulfilled. It seems more likely that an appraisal of the value of antihistaminic drugs will eventually be arrived at by the study of large, controlled groups of patients by a number of investigators in different places, basing conclusions principally on symptomatic relief obtained by drug or placebo. One such study (on a small scale, however) using Neo-Antergan® was carried out at the student health service of the University of California Medical Center between September 1948 and April 1949, with the results shown in Table 2.

Another much larger controlled study carried out on an industrial population in California gave similar results.[4]

These three controlled studies (excluding that of Arminio and Sweet[3] because of doubtful interpretation) all show a difference of approximately 15 to 20 per cent between control and drug-treated groups, in favor of the drug (Table 3). If it be assumed that from 10 to 30 per cent of all so-called "colds" may have a strong allergic or "vasomotor" component in which antihistaminic drugs would be expected to be beneficial, it must be concluded that antihistaminic agents do not cure the majority of cases of the common cold.

A very recent well-controlled study at the United States Military Academy[17] showed no essential difference in results between the treated and control groups. Treatment was not generally begun until some hours after onset of symptoms. This tended to exclude patients with transient symptoms — the group on which the proportion of spontaneous cures is likely to be highest.

TABLE 2

Medication	Number of Patients	Relief	No Relief	Undesirable Side Action
Drug	45	19	26	22
		42%	58%	49%
Placebo	47	12	35	14
		26%	74%	30%

TABLE 3

Investigators	Control Group: No. of Patients	Control Group: Per Cent Failure	Treated Group: No. of Patients	Treated Group: Per Cent Failure
Brewster[6]	140	47	694	25
Beard[4]	94	44	140	29
Talbot and Jawetz	47	74	45	58

After a thorough study of all available data on the therapy of the common cold one is inclined to remember an account of therapy used more than 50 years ago:[7] "We were rubbed lavishly with hot grease" . . . "stinging plaster made of mustard and white flour" was applied . . . "We used to sit for half an hour before bed-time with our feet in a pail of hot mustard water. Then we were put to bed surrounded by hot soapstones, and in the morning we were damp but cured." It seems doubtful whether modern science has much more to offer in the treatment of the common cold.

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Intestinal Obstruction

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SUMMARY

Despite improvements in knowledge of the pathologic physiology of intestinal obstruction, the introduction of gastrointestinal decompression, and more effective antibiotics, obstruction remains a serious disease with a high mortality rate. Although the diagnosis is often obscure, it can usually be made with a fair degree of accuracy by the history alone; pain is fairly constant and characteristically is of a cramping type simulated by very few other lesions. Distention is present in low lesions but absent in high lesions; on the contrary, vomiting is minimal in low lesions but prominent in high lesions. Visible peristaltic waves are almost pathognomonic of intestinal obstruction. Increased peristaltic sounds, as noted by auscultation, are extremely helpful in diagnosis; they are absent in paralytic ileus.

Although intestinal obstruction is a surgical lesion, it must be remembered that in the type produced by adhesions the obstruction can be relieved by gastrointestinal decompression in 80 to 90 per cent of cases. Operation is usually indicated a short time after relief because of the probability of recurrence. In practically all other types of obstruction decompression is indicated only while the patient is being prepared for operation. Obviously any type of strangulation demands early operation. Strangulation can usually be diagnosed, particularly if it develops while the patient is under observation. Increase in pain, muscle spasm and pulse rate are important indications of development of strangulation.

Dehydration and electrolytic imbalance are produced almost universally in high obstruction. Usually, it is unwise to wait until these two deficiencies are corrected before operation is undertaken, but correction must be well under way at the time of operation. Resections should be avoided in the presence of intestinal obstruction, but obviously will be necessary in strangulation. Operative technique must be expert and carried out with minimal trauma. Postoperative care is very important; important features are decompression, for two to three days, accurate fluid and electrolytic replacement, and transfusions.

THE medical profession has always realized that intestinal obstruction is a serious disease carrying with it a high mortality rate. Fortunately, the mortality rate has decreased sharply during the past several years. Much of this improvement in results has been related to intelligent use of intestinal decompression. It must be emphasized, however, that unless decompression is utilized intelligently, the mortality rate may actually be increased. Although there are two types of obstruction, namely mechanical and functional, the material in this presentation will be confined largely to the former type. Surgeons, of course, realize the frequency of functional obstruction (for example, paralytic ileus) because it is so common after celiotomy. It is likewise encountered in abdominal trauma and notoriously develops after retroperitoneal injury.

The incidence of the various types of obstruction varies considerably in different reports, depending largely upon the percentage of patients derived from an emergency service; for example, in a city hospital where the percentage of emergency cases is high, the incidence of strangulated hernia will be high, whereas in private hospitals, where a relatively small number of emergency cases are received and where the number of patients admitted for operation is high, the incidence of obstruction due to adhesions will be high. A summary of numerous reports in the literature is given in Table 1.

From the Department of Surgery, University of Illinois College of Medicine.

Guest speaker's address delivered before the First General Meeting of the 79th Annual Session of the California Medical Association, April 30-May 3, 1950, San Diego.

DIAGNOSIS

If the patient is questioned carefully regarding certain points in the history, the diagnosis of intestinal obstruction can usually be made within a few

TABLE 1.—*Incidence of Types of Obstruction* (summarized from the literature).

	Per Cent
Strangulated external hernia	33
Obstruction due to adhesions (¾ are postoperative)	32
Obstruction due to neoplasm	15
Intussusception	8
Volvulus	3
Internal hernia	2
Foreign body (gallstones, etc.)	1
Miscellaneous causes (congenital anomaly, mesentery thrombosis, etc.)	6

minutes. The most important diagnostic aid lies in the type of pain. With few exceptions, the pain of intestinal obstruction starts out as a true cramp which is mimicked by few other diseases. In other words, the cramp develops for a minute or two and gradually disappears, remaining absent for a variable length of time, perhaps one to five minutes. Commonly a moderate amount of mild diffuse pain remains between cramps. This is particularly true if the obstruction has been present for a considerable time, and when strangulation is present.

Examination of the abdomen is usually very helpful, as an intestinal pattern and peristaltic waves will almost always be demonstrable unless the abdominal wall is very obese. If the distention is severe, the abdominal wall may be tense, but muscle spasm is absent unless strangulation is present. Vital information can be obtained by auscultation of the abdomen. Almost always there will be increased sounds unless peritonitis is present. However, since the intestinal sounds are not constant but manifested only during peristaltic waves, it is usually necessary to listen for three to four minutes before an accurate assay can be made as to the amount of accentuation.

On numerous occasions, particularly in the postoperative care of patients, it will be extremely difficult to differentiate between postoperative ileus and mechanical obstruction. However, in the former complication pain is minimal and peristaltic sounds either absent or minimal; likewise peristaltic waves are not seen in postoperative ileus. Differential diagnosis may be extremely difficult if the mechanical obstruction is complete, in which case distention would be minimal and pain variable. X-ray examination is of extreme aid in diagnosing intestinal obstruction. However, with few exceptions the examination must be limited to a plain film of the abdomen or to films with barium enema; ordinarily, barium by mouth is strongly contraindicated unless it is known that the obstruction is in the pylorus or duodenum and the barium can be aspirated immediately after the examination is completed. A variable amount of fluid is found in the free peritoneal cavity. In the absence of strangulation it is clear and relatively scanty. It has a high protein content similar to that of blood plasma.

Symptoms of shock may develop late in intestinal obstruction. They are related to the loss of fluid which may be as great as 5 to 6 per cent of the body weight. Occasionally the shock is related to the development of strangulation of a large loop of intestine; in this instance a large amount of blood along with fluid would be trapped within a very short time, thereby reducing the blood volume rather abruptly. When perforation through a gangrenous area takes place, shock is likewise common. In these circumstances it is due largely to the absorption of toxic products escaping into the free peritoneal cavity.

High Intestinal Obstruction. Although pain is the first symptom of intestinal obstruction, nausea and vomiting develop early if the obstruction is high, that is, above the ileocecal valve. When the obstruction is located in the duodenum, distention may be minimal because only the stomach is involved. However, on rare occasions when chronic obstruction of the duodenum is present the stomach becomes so dilated as to completely fill the abdomen when filled with gas and fluid. When the obstruction is located lower in the small intestine, a variable amount of distention will develop, depending largely upon the amount of vomiting. Constipation is of course a symptom of intestinal obstruction, but when it is located high it should be emphasized that the patient may have one or two bowel movements several hours after the development of obstruction because the portion of the intestinal tract distal to the obstruction can be emptied as usual.

Dehydration and hypochloremia develop in high intestinal obstruction at a rate depending largely upon the amount of vomiting. Dehydration naturally results in diminished blood volume and decrease in urinary output, which in turn results in elevation of the non-protein nitrogen level. The diminished blood volume is accentuated by the loss of plasma through the lumen and wall of the intestine.

Figure 1.—Plain film of abdomen reveals distended loop of intestine with a "herringbone" pattern typical for small intestine. The patient, aged 30, had a cesarean section 12 days previously and had abdominal pain with nausea and vomiting for two days prior to admission. Decompression was effective; the tube was removed in 24 hours and feedings begun. Obstruction recurred and operation was performed. An adhesion at the suture line was found obstructing a loop of mid-ileum. Decompression longer than 24 hours might have resulted in relief lasting at least for several days, thus allowing restoration of the physical condition to normal. Operation could then have been performed in an interval phase when the operative risk was optimum.

X-ray studies are of great value in the diagnosis of high intestinal obstruction. When the obstruction is proximal to the ileocecal valve loops of the small bowel will be distended but there will be no distention of the large bowel. Distention of the small bowel is associated with a rather typical herringbone pattern on the x-ray film (see Figure 1). Fluid levels are likewise usually observed.

Low Intestinal Obstruction. In low intestinal obstruction the pathologic changes differ from those in high intestinal obstruction, largely because vomiting is minimal or even absent. It is not uncommon for a patient to have low obstruction for a period as long as four to five days and with a history of having vomited only once or twice during that period. However, the dehydration still develops with a variable amount of hypochloremia due largely to lack of intake of water and food. Distention itself is an extremely dangerous complication of obstruction. It may actually cause gangrene although gangrene is usually caused by compression of vessels by a hernial ring or other mechanical process. When compression is applied to the wall of the intestine, whether it is produced by an extrinsic mass or gaseous distention, the veins will be obstructed before the arteries, primarily because they are more collapsible and usually located in a more superficial position. Obstruction of the veins permits the accumulation of fluid in the wall of the intestine and in the lumen because of transudation. Sperling has shown in experimental studies that gangrene can be produced if a pressure of 20 cm. of water is maintained in the lumen of the intestine for a period of 24 hours. Most patients with low intestinal obstruction appear quite ill, and notoriously tolerate operation poorly. This debilitation is no doubt related in some way to the extreme distention, but the exact mechanism is unknown, unless the anoxia in the bowel wall produced by the distention gives rise to toxic products in the wall of the intestine itself.

Constipation will of course be a prominent feature in low intestinal obstruction; rarely will there be a bowel movement after complete obstruction develops. Occasionally bloody discharge in the rectum may be noted and it may be expelled. However, this is so uncommon as to be of little value diagnostically except in infancy when conditions such as intussusception are associated with bloody discharge. As in high intestinal obstruction, a plain x-ray film will be very helpful in diagnosis. If the obstruction is limited to the left side of the colon, considerable large bowel distention may be observed (see Figure 2). Obstruction is quite infrequent in carcinoma of the right colon, but is common in carcinoma of the transverse colon. When there is considerable doubt in the diagnosis, a barium enema is permissible to establish diagnosis, although the barium should be removed by a rectal tube and the bowel irrigated after the x-ray examination. If barium is forced under pressure past an obstruc-

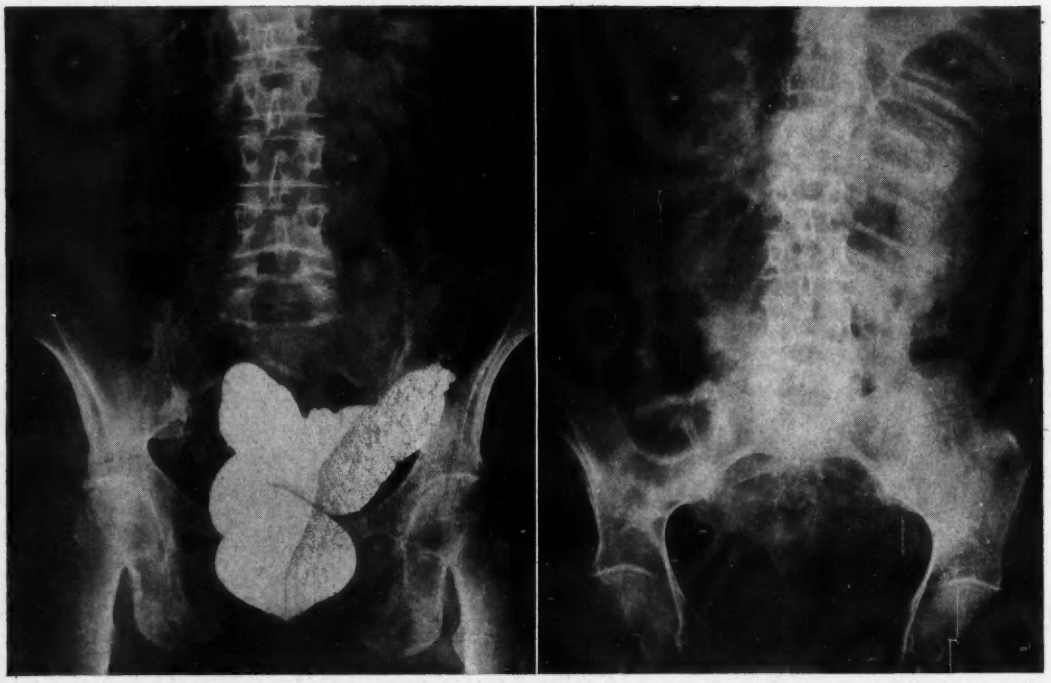

Figure 2.—*Left:* Plain film of the abdomen in a patient, aged 58, with evidence of complete intestinal obstruction for three days but with a history of having vomited only once. Distention was pronounced. Note the distended loop with haustral markings typical for large bowel. *Right:* Same patient. Barium enema revealed an obstruction in the sigmoid colon. A diagnosis of carcinoma was obvious.

tion, it may be retained for a considerable time and greatly complicate surgical treatment (see Figure 3).

DIAGNOSIS OF STRANGULATION

Although it is usually quite difficult to diagnose strangulation in patients who are admitted in emergencies, it can usually be detected when it develops in patients who have been under observation for several hours. It is so important to determine the presence of strangulation as soon after development as possible that the manifestations are listed below in some detail.

1. An *increase in the amount of pain* is one of the most valuable indications of the development of strangulation. This is particularly true when the pain is superimposed on the abdominal cramps. Notoriously the pain of strangulation is much more severe than that of simple obstruction; it may be so severe that the patient pleads for narcosis.

2. An *increase in abdominal tenderness* invariably develops along with the increase in pain. It is usually but not invariably located at the site of pain.

3. An *increase in pulse rate* is almost always found when strangulation develops. It is due in part to the development of pain but is accentuated by the loss of blood through the strangulated loop.

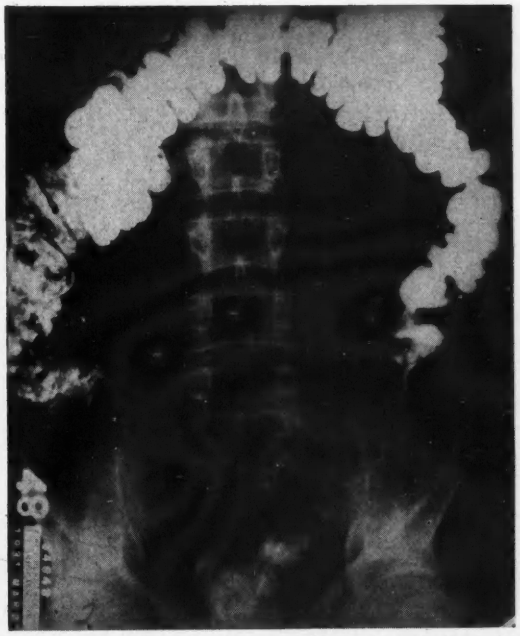

Figure 3.—The patient had a history of cramping pain and alternate attacks of constipation and diarrhea. Distention was present at intervals. A diagnosis of partial obstruction of the large bowel, due probably to carcinoma, was made. A barium enema revealed a constricting lesion in the sigmoid colon; under moderate pressure the barium passed the obstruction and filled the rest of the large bowel. The film shown above was taken 48 hours after the barium enema and after evaluation along with a soapsuds enema. Note the pronounced retention of barium proximal to the obstruction. This complication will usually prevent consideration of resection with primary end-to-end anastomosis, because the desiccated masses of barium can usually not be washed out with enema or colonic irrigations.

4. The development of a *mass* strongly suggests the presence of a strangulated loop which becomes so distended as to appear firm to palpation. Obviously the mass will not be palpable if the strangulation involves merely a small area of intestine such as that produced by an adhesive band.

5. The development of *muscle spasm* in simple strangulation is somewhat variable but usually is present to a slight degree soon after the strangulation develops. The amount of intestine strangulated may exert a slight influence on the development of muscle spasm but by no means is the amount of spasm dependent upon the amount of intestine involved in the strangulation. A most important factor in the development of muscle spasm is perforation through the gangrenous wall.

6. *Leukocytosis* usually develops comparatively early in strangulation. The number of leukocytes per cubic millimeter may be no greater than 10,000 to 14,000 until peritonitis develops, when it may rise sharply to 25,000 or 30,000.

7. A *sudden fall in blood pressure* is sometimes indicative of the development of strangulation in a long loop of intestine which may have been obstructed for several hours preceding the strangulation. It may also indicate perforation, since it is encountered in other lesions such as hemorrhage. Fall in blood pressure alone is not diagnostic of strangulation. It is, nevertheless, a sign of serious complication, and usually indicates that surgical treatment is urgently needed. Fever is usually present in strangulation although it may also be produced by dehydration. However, the temperature is rarely very much elevated unless peritonitis is present.

The physician must not wait for all of the manifestations listed before diagnosing strangulation. As a matter of fact, when fever or leukocytosis develops, peritonitis is commonly already present, and the patient is liable to die regardless of the type of therapy instituted. Perhaps the earliest signs of strangulation are increase in pain and increase in pulse rate. When these two symptoms develop, the possibility of strangulation must be considered. If there is any doubt about the possibility of strangulation while the patient is undergoing conservative treatment, it is usually advisable to resort to celiotomy rather than to wait until the manifestations are obvious (see Table 2).

TABLE 2.—*Contraindication for Continuation of Nasal Suction in Intestinal Obstruction.*

1. Increase in abdominal pain.
2. Increase in abdominal tenderness.
3. Increase in pulse rate.
4. Development of a mass.
5. Development of muscle spasm.
6. Failure to obtain relief of distention.
7. Leukocytosis.
8. Fever.
9. Sudden fall in blood pressure.

TREATMENT

Decompression. The treatment of intestinal obstruction is dependent upon the type of obstruction. With the utilization of the principle of decompression advocated by Wangensteen, almost all types of obstruction now can be much more intelligently treated. As a matter of fact, obstruction due to adhesions can be completely relieved in 80 to 90 per cent of cases, but only if decompression is utilized intelligently. Decompression is likewise very effective in functional ileus; operation is obviously contraindicated in obstruction of this type.

Accordingly, decompression can be utilized as a definitive method of treatment in functional ileus and obstruction due to adhesions. However, it is very seldom effective in such lesions as carcinoma of the colon, volvulus, intussusception, extrinsic mass, and stricture. It is obvious that some of the latter named lesions, including intussusception and volvulus, must be treated by emergency operation as soon as the patient's condition can be brought to that of reasonable operative risk. However, in obstruction of that type, where immediate operation is mandatory, decompression should be instituted as soon as the patient is admitted to the hospital so that the stomach and upper jejunum may be evacuated, thereby facilitating anesthesia as well as reduction of distention. Moreover, early decompression will prevent further development of distention by removing all swallowed air.

Therefore, it is always good therapy to institute decompression immediately after admission to the hospital even though the exact type of obstruction is still unknown. Opinions differ as to the type of tube to be utilized in decompression. In general there are three types (see Figure 4). The Miller-Abbott tube, the Harris tube and the Cantor tube are actually superior to the Levine tube placed in the stomach because decompression can be achieved down to the point of obstruction. Unfortunately it is sometimes very difficult to pass the tube beyond the duodenum. It is true that the Harris tube, weighted with mercury at the tip, is usually passed more easily than the Miller-Abbott tube. An added advantage of the Harris tube is that it has a large lumen. This minimizes blocking of the tube with food particles—a serious complication which if not appreciated can defeat the value of decompression. Often it may be desirable to insert a large stomach tube to wash out all food particles from the stomach and then insert a smaller tube for decompression. Even so, it is essential that the decompression apparatus be inspected frequently during therapy to be sure that decompression is being carried out.

As previously indicated, decompression therapy can be considered as definitive treatment when the obstruction is due to adhesions. After good decompression is obtained, the obstruction may be relieved, although the tube must not be removed too early. In general it is rare to obtain significant relief of obstruction in less than two or three days. Accordingly, the tube must be kept in for at least that long even though it may appear obstruction has been relieved. After it is obvious that obstruction has been relieved, the tube can be removed and the patient permitted to take water by mouth. Liquids and soft diet can be given thereafter, but only in small, gradually increased amounts. Although decompression may relieve the obstruction, it is liable to recur when the patient resumes a normal diet. This recurrence is so common that it is usually advisable to operate for correction of obstruction during the interval of relief.

Operative Treatment. Careful judgment must be exercised in determining the time for operation in intestinal obstruction. As previously noted, in many cases in which the obstruction is produced by adhesions it will be relieved by decompression alone. However, on most occasions it will be necessary to operate after food intake has been resumed because obstruction is so liable to recur.

Except in paralytic ileus and obstruction due to adhesions, operation will be necessary as soon as the patient is in condition to withstand the procedure. Even though strangulation of the intestine is obvious, it is always necessary to correct such decrements as dehydration and loss of electrolytes. Although the usual rate of introduction of intravenous fluid is 500 cc. per hour, this rate may be increased greatly in the presence of dehydration, unless there is a history of cardiac disease. Accordingly it may require four to six hours to improve the patient's condition to the point where he will tolerate the operation with moderate safety.

There are no accurate rules regarding the amount of fluid and electrolyte to give the patient with obstruction, but certain general principles are agreed upon. For example, when dehydration is present, fluids are given rapidly and the urinary output measured every few hours. Until the urinary output is equivalent to at least 50 cc. per hour, it may be assumed that dehydration still exists. The solution usually used to overcome dehydration is 5 per cent glucose with normal saline solution. However, it must be emphasized that once the electrolyte deficiency has been corrected, administration of saline solution in the immediate postoperative period should be carried out cautiously, particularly in patients whose kidneys are perhaps damaged by arteriosclerosis or other disease. Coller's formula, which states that 0.5 gm. of sodium chloride per kilogram of body weight may be administered for each 100 mg. of chloride deficiency per 100 cc. of plasma, can be used, but with caution. Only in young individuals with normal kidneys can this formula be used with safety. It should be emphasized that in elderly people whose kidneys are functioning below normal, it is unsafe to give the amount of salt called for in the formula, particularly if operation is to be carried out immediately, lest salt retention cause oliguria or anuria postoperatively.

Many patients with intestinal obstruction will need a transfusion of blood before or during the operation. Determination of hemoglobin value, packed red cell volume and erythrocyte count at the

time of admission of the patient will yield misleading data; because of dehydration and reduced plasma volume, the values will be relatively high. Accordingly these determinations must be repeated in three to four hours after hydration is carried out, in order to obtain information on the real status of the blood. If, for example, results of blood studies on admission are normal findings, or if results of examination of the blood drawn three to four hours later (before complete hydration has taken place) are slightly below normal, it may be assumed that the patient actually is anemic and should be given blood before as well as during operation.

Certain principles in the operative treatment must be recognized and respected. Manipulation of the intestine must be held to a minimum. If strangulation is present, superficial exploration of the abdomen will almost invariably reveal its location. Obviously, if a condition such as intussusception is present, superficial palpation will reveal a mass, thereby making further exploration unnecessary. In the absence of a mass or obvious location of the obstruction, it may be necessary to examine various loops of intestine. If decompression has been quite effective, there may not be significant dilation of the intestine proximal to the obstruction. However, in ordinary circumstances the surgeon may be guided by observation of dilated loops proximal to the obstruction and collapsed loops distal to the obstruction. Frequently, indeed, observation of such conditions will lead the surgeon rapidly to the point of obstruction.

In general, if there is active obstruction, resection should be avoided if possible, but obvious gangre-

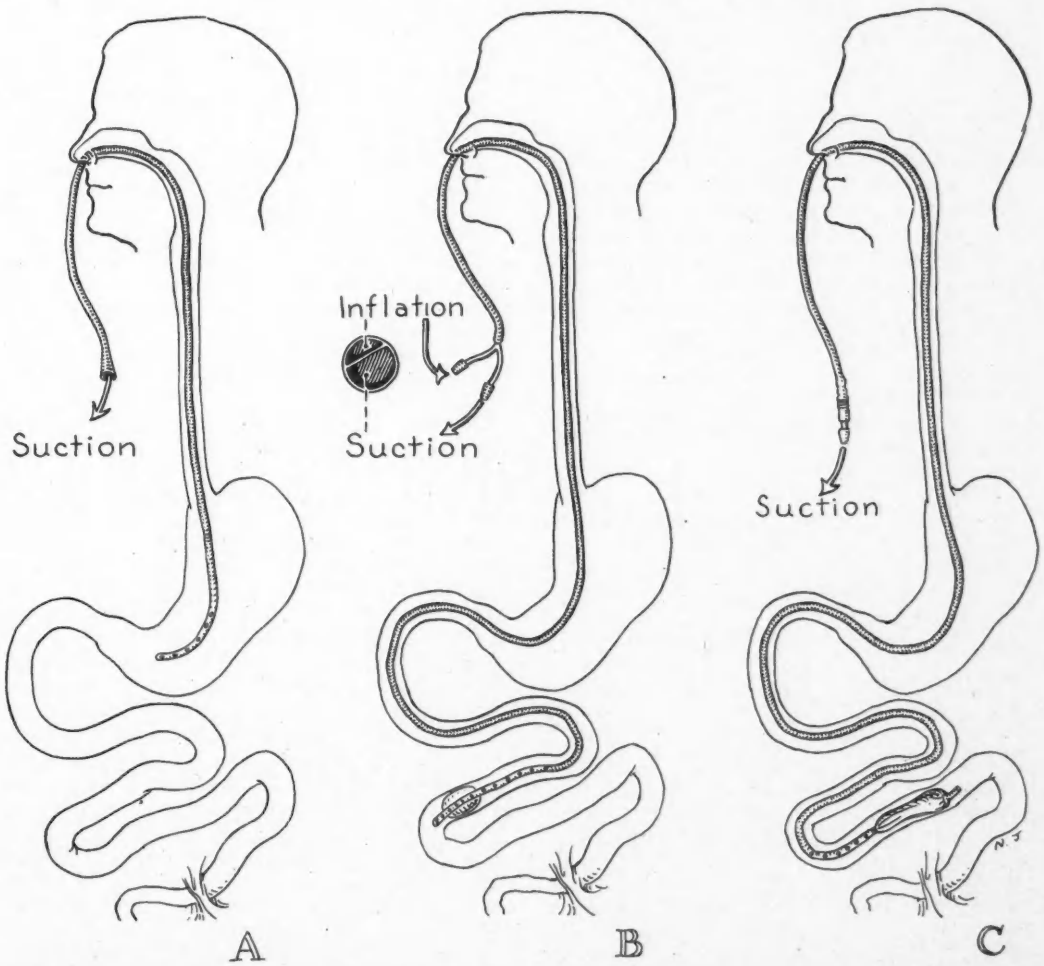

Figure 4.—Three types of tubes are available for gastrointestinal decompression: (a) Ordinary Levine tube inserted through the nose into the stomach. (b) The Miller-Abbott tube can be passed through the duodenum down to the point of obstruction. The tube contains two lumina as indicated by the insert. The balloon at the tip contains air. (c) The Harris tube can be passed down to the point of obstruction; it has an advantage over the Miller-Abbott tube because it has a large (only one) lumen for evacuation of fluid and food particles. The rubber balloon at the tip contains mercury (after Cole in Canadian Medical Association Journal).

nous loops of intestine or loops without viability cannot be returned to the peritoneal cavity. When resection is done, it will occasionally be life-saving to bring the strangulated loop outside the peritoneal cavity as an obstructive resection. The wound then may be closed around the two branches of the loop. This procedure is much more applicable to obstructed strangulated loops in the large bowel than to those in the small bowel because the postoperative loss of fluid and electrolyte from the small bowel is so much greater than from the large. (It should be noted in passing that resections can be carried out more boldly than in the past, provided adequate blood is given during and after operation.)

Another precaution which must be respected at all times is that anastomosis must not be carried out in an area where the intestine is edematous. In other words, the resection must be wide enough so that the anastomosis can be performed through relatively normal intestine.

POSTOPERATIVE TREATMENT

With very few exceptions, gastrointestinal decompression must be instituted after operation. If the Miller-Abbott tube or Levine tube was functioning before operation, it should be left in during and after operation. This will maintain decompression so that pressure of distention against a suture line will be prevented. How long to continue decompression after operation cannot be determined by a simple rule. However, with few exceptions, it must be maintained for 48 hours after resection and anastomosis have been carried out. After 48 hours, if a moderate amount of distention is present, perhaps because of inefficient decompression, it may be necessary to continue decompression for another day. Occasionally when the tube is removed and the patient is given fluids by mouth, distention reaccumulates. In such circumstances it may be necessary to replace the tube after 24 to 36 hours. Auscultation of the abdomen may help in determining when to remove a tube or to begin feedings: Once peristaltic sounds return to normal, food intake should ordinarily be tolerated satisfactorily unless obstruction exists.

As was intimated previously, the blood picture must be followed closely and transfusion carried out if the protein content or the erythrocyte count is below normal.

RESULTS

The mortality rate in intestinal obstruction before the institution of gastrointestinal decompression was as high as 35 per cent. It varied somewhat depending upon the number of strangulations in the respective series. At present the mortality rate is between 10 and 15 per cent for a large series of patients. This improvement is due largely to decompression, a more judicious use of blood, a better understanding of fluid and electrolyte balance, and the use of chemotherapeutic agents. Naturally, the duration of obstruction affects the mortality rate. For patients receiving care within 24 hours of the onset of symptoms, the mortality rate should be as low as 5 per cent.

Virology of Poliomyelitis

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SUMMARY

The virus of human poliomyelitis has been demonstrated in excretions before onset of the disease, during the disease, and in convalescence. It may be confused with different viruses likely to be found in the same sources in clinical conditions resembling poliomyelitis.

Immunologic differences between strains of poliomyelitis virus have been detected so that three types are now evident. The distribution of these types and their importance as causes of epidemics are not known. This multiplicity of immunologic types is an important factor in considering immunization of humans. Commercial manufacture of vaccines faces many technical problems.

Recently the Coxsackie virus has been demonstrated in humans with a disease closely resembling poliomyelitis.

THE infective agent of poliomyelitis has been defined in terms of its source, its pathogenicity for a limited host range, the pathologic and histologic features of the changes it causes in human and primate hosts, and its immunologic characteristics.[26] It has recently been given generic and specific names, *Legio debilitans*, in an effort to bring some order out of the chaos in the field of virus taxonomy.[5] This effort was probably not entirely justified by the stage of development of information on the subject. It is to be hoped, however, that this step will lead to the development of a more widely acceptable scheme of classification of the neurotropic viruses. This presentation will be largely confined to discussion of the virus of human poliomyelitis. Other viruses possibly of significance in human disease will be touched on briefly; the so-called Coxsackie virus will be discussed more especially.

Excretion of poliomyelitis virus during the course of infection and by carriers has been the subject of much important investigation in the past. The virus is demonstrable in the naso-oropharynx during four or five days prior to onset of symptoms and perhaps for as long as ten days after. It is also excreted in the feces for as long as four months after onset although less than 25 per cent of convalescent patients shed the virus past the sixth week.[28] The virus may be found in the feces some days prior to onset. The longest period so far observed was 19 days.[6] Where the virus is elaborated has not yet been determined. It has been demonstrated in the walls of the intestine and in mesenteric lymph nodes of experimental animals and of man.[34] It has also been found in tonsils.[17] The suggestion is strong that the wall of the alimentary tract is the primary site of invasion as well as the point of major excretion from the body. The virus has been demonstrated in peripheral nerves of experimental monkeys by electron micrography.[11] Children are more likely to excrete the virus than are adults, and the stools of young family contacts of patients are more liable to contain the virus than are the stools of adults of the family.[28] The virus was found in stools and throats of six out of ten patients with mild "summer grippe" occurring in an epidemic among children.[31] Recently, another virus, Coxsackie virus, has been isolated by inoculation of infant mice with pharyngeal and fecal excretions from patients who had symptoms closely resembling those of poliomyelitis.[9, 10] This agent has been detected in several sections of the country and like the poliomyelitis virus apparently has a wide geographic distribution.[8]

A number of other viruses have been described which resemble human poliomyelitis virus and which have been found under circumstances that allow of considerable doubt as to their etiologic connections with the human disease. Some confusion has been created in the past by the fact that some of these viruses have been regarded by certain workers as "models" of human poliomyelitis virus. The virus of mouse encephalomyelitis (Theiler virus), Columbia SK, MM, and encephalomyocarditis viruses can be listed in this group of infective agents.[26] They are probably primarily parasitic in lower animals, some occasionally attacking man, others probably never causing human disease.

Large scale investigation of the subject of differences that might exist among various strains of human poliomyelitis virus has for many years been hindered by the expense of experimental animals and the rather academic nature of the problem. Recently, however, greatly increased interest has been shown in the possibility of artificial immunization against the clinical disease, and as a consequence animals in plenty have become available for solution of a problem that may have retained its academic character but has acquired a very practical stature. Work on this problem during the past two or three years has brought to light that there

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are at least three major types or varieties of poliomyelitis which infect man.[1, 2, 3, 14, 16, 18, 23, 24, 30] Techniques include challenge of convalescent immune monkeys with large doses of viruses from different sources. By using two immunologically different viruses as prototypes, three types can be distinguished. Preliminary experiments with neutralization tests using serum from monkeys immunized with the prototypes have indicated that the same viruses fall in the same three types. Another technique in process of development has yet to be put to this use; this involves flocculation of purified viral antigens in specific immune sera, and the test is performed *in vitro*.[30] Yet to be determined (and of epidemiologic importance) is the geographic distribution of types over the world, the percentage occurrence of types in epidemics, and which types are to be found in carriers.

If vaccines capable of conferring adequate immunity are to be manufactured, distributed, and administered on a scale wide enough to curb the disease, several questions other than those regarding immunologic type differences must be answered. One is: Are killed or inactivated viruses immunogenic? Some work along this line[20, 22] indicates that formalinized virus preparations do provoke resistance to homologous test virus given intracerebrally. Another question is: How much overlapping immunity is produced by virus of one type as vaccine against another type? So far, indications are that little if any such cross-immunity is established, even with living vaccines,[1, 2, 3, 16, 18] although there is some suggestion that the death rate in animals paralyzed for a second time is lower than the rate in control groups (unpublished data). There is some evidence[25] that the immunity of infected animals is different from immunity of vaccinated animals and it has been suggested that this immunity to infection resides in the tissue of the central nervous system. This work has not yet been confirmed, however, so that the role of tissue antibody in resistance and even its existence are still in doubt.[32] Although considerable work has been done on the problem of attenuating or altering the virulence of a poliomyelitis virus to make it a safe vaccine in the manner of smallpox vaccine, yellow fever vaccine, and others, no such product is immediately forthcoming. Another problem in the manufacture of a vaccine is its source. Spinal cords of infected monkeys have thus far served for experimental vaccines, but obviously this supply is too limited. Promise for solution of this problem is offered by the development of a technique for culture of human poliomyelitis virus in infantile human tissues, not restricted to nervous tissue and including skin.[12] This may lead to *in vitro* methods suitable for large-scale commercial production. The use of some chemical or physical method for purification and concentration of the virus would be a great help to settle the problem of source of vaccine. A recent report demonstrated that poliomyelitis virus can be concentrated to some extent and somewhat freed of extraneous brain tissue material by processing with protamine sulfate.[35] The problem of demyelinating encephalomyelitis as a postvaccinal complication will necessitate use of methods to remove the encephalitogenic factor from vaccine made from central nervous system tissue. This problem is under active investigation in connection with rabies vaccine manufacture, and a recent report states that some success has been achieved in an experimental method for removing the troublesome fraction.[13]

Problems presented by this disease have been enhanced recently by the discovery of another viral agent (previously mentioned) which is present in secretions of the nose and throat and in feces[9, 10] of patients with paralytic or non-paralytic disease resembling poliomyelitis. This agent was found in feces of non-paralytic patients during an epidemic of poliomyelitis.[8] It was also found in the feces of some of the previously mentioned patients with "summer grippe"; and when monkeys were inoculated with preparations from the feces of those patients, typical poliomyelitis virus was recovered from the monkeys. So the two viruses may co-exist.[21a] Accidental laboratory infections with this virus have resulted in a disease with symptoms of pleurodynia. Neutralizing antibodies developing during convalescence are distinguishable from antipoliomyelitis antibodies. Five antigenic types of the virus have been defined on the basis of complement-fixation tests.[7, 15, 33] The influence of these findings on the future control of poliomyelitis cannot yet be assessed. Monkeys are not infected experimentally with this virus except for the cynomolgous monkey, in which a mild disease resembling experimental non-paralytic poliomyelitis develops.[21]

Thus, a more thorough understanding of the virology of poliomyelitis is necessary for an intelligent approach to the problems of the control of the disease. And at present data are being gathered in various cooperating and also independently operating laboratories in order that this goal may be achieved.

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Diagnostic Problems in Poliomyelitis and How They Are Met

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SUMMARY

A brief review of salient facts pertaining to poliomyelitis is presented as an introduction to the other articles which follow, each a part of a symposium concerning this clinical entity in its various phases.

POLIOMYELITIS is divided into three clinical groups, abortive, non-paralytic, and paralytic. As long as fever persists, the disease may progress from one of the less severe categories to the graver. It is probable that in non-epidemic periods many cases of a sporadic nature are diagnosed incorrectly. During epidemics, physicians are more alert to the probability of the occurrence of the disease, and increasing experience at such times sharpens diagnostic acumen.

At present there is no method by which abortive poliomyelitis may be accurately diagnosed. Diagnosis must rest purely upon epidemiological grounds, suspicion, and inference. As in healthy typhoid or diphtheria carriers who have never had symptoms of these diseases, infection with poliomyelitis virus may produce no evidence of disease in the host. Howe[4] stated that 100 cases of abortive poliomyelitis occur for each diagnosable case that is reported. Formerly, this incidence was believed to be much less; it is probably very much higher. In a careful study made during 1948 in Auckland, Thompson[6] found the over-all ratio of suspect illness to positive diagnosis to be 300:1. In a house-to-house canvass, he accepted as abortive cases those in which the start of illness fell within six days on either side of the onset of illness in a known poliomyelitic contact. He found the chief symptoms to be fever, headache, vomiting, diarrhea, and sore throat, in many instances accompanied by pain or stiffness in the neck, drowsiness, abdominal pain, and delirium. (In the author's experience, low lumbar backache has been noted more frequently; and it has also been observed that departure from normal bowel habit, either diarrhea or constipation, varies with different epidemics or may be absent. Delirium has not been observed.)

It has been believed that changes in the spinal fluid do not occur in abortive poliomyelitis cases. Such is not always the case, for occasionally the author has noted both increased protein content and cell counts in the spinal fluid of patients who had no detectable signs of muscle weakness or reflex changes. On the whole, however, it is best to consider those cases abortive in which no clinical evidence of central nervous system involvement is present, the picture being that of a mild, short, nonspecific illness. However, that infection is present has been shown by the presence of the virus in the stools[2] of some of these patients at a time when rises in titer in the antiviral properties of the blood also developed.

Patients with non-paralytic poliomyelitis have transitory signs of paresis or mild paralysis from which they rapidly recover. The onset of the disease is like that of the paralytic form, the degree of severity varying from patient to patient. As in the paralytic cases, the course of the disease may be either monophasic (four-fifths of the cases) or biphasic (one-fifth of the cases).

While the biphasic type may occur at any age, it is commonest in the age group five to nine years inclusive. It is rare in very young children. Outside the age bracket of greatest incidence, most of the remainder of such cases occur in adults. In those cases in which the course of the disease is biphasic, diagnosis cannot be made until evidence of central nervous system involvement develops. In the majority of cases, however, the onset of poliomyelitis is without any distinct phase, and either is abrupt or develops gradually over a period of a few days, with severe headache, moderate or low fever, stiffness of the neck, stiffness or pain in the low back, vomiting, and constipation or diarrhea, although frequently no bowel change is noted that is not consistent with anorexia and lack of food intake. (Symptoms with reference to the bowel vary in different epidemics; diarrhea was frequently noted in those cases occurring in Los Angeles during the third decade of this century.) If the patient flexes his neck to bring the chin against the chest, the maneuver elicits pain either in the neck or in the lumbar area. Frequently the patient cannot accomplish the flexion, and when it is done by the physician with the patient recumbent, the knees draw up (Brudzinski's sign). Likewise, if the patient can sit erect with legs straight before him on the bed, he cannot reach forward and touch his toes, nor can he bend his back to place the head between his knees. Head drop also may be present. Mild paresthesias are not uncommon. Changes in the superficial reflexes usually occur first, then in the deep reflexes, and finally paresis or paralysis. Tightness in the muscles of the back and hamstrings becomes apparent. (This is

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commonly called spasm, although neurologists uniformly object to this appellation upon etymological grounds.) The onset of the usual case of poliomyelitis and that of the second phase in the biphasic type are alike in all respects. The pulse is disproportionately rapid in relation to fever and often remains fast after fever subsides.

In the biphasic cases, the first phase is one of minor illness during which the virus is producing a systemic disturbance,[5] probably multiplying in the alimentary tract, just as in the abortive type which does not go on to a second phase in which the nervous system is involved. This first phase is not to be construed as prodromal, or as a preceding separate and distinct illness, for the virus is present and active in the host at this time, and may be proven present in the stools. The symptoms of the first phase are the same as those of abortive poliomyelitis. These symptoms last for a day or two, then disappear. After an interval averaging four days, the second phase follows.

The author has never known vigorous exercise, when taken at or about the time of onset, to increase the severity of the illness in patients who subsequently had what was believed to be abortive poliomyelitis. The same may be said with regard to patients who actually were in the first phase of the biphasic type. On the other hand, such exercise at the onset of the second phase of the biphasic disease, as well as in all types of monophasic poliomyelitis, appears to increase the severity in nearly every instance—probably causing the death of some patients who otherwise might have survived.[3]

When the virus attacks the nervous system, the changes it produces can be observed at autopsy in some degree from the forebrain to the cauda equina. Such changes also have been repeatedly observed in the dorsal root and the various sympathetic ganglia, in the sympathetic fibers accompanying blood vessels, and in the lateral column of Clarke, as well as in the anterior horn of the cord. It must be apparent, therefore, that symptoms will vary as the disease progresses, depending upon the virulence and quantitative multiplication of the virus at different levels in the central nervous system. It must be apparent also that all manner of combinations may be present: The lumbar cord with one or both legs involved; the cervical cord, with one or both arms, or the phrenic nerves and paralysis of the diaphragm; ascending types like Landry's paralysis; descending types, rarely mentioned in the literature; involvement of the trunk with muscular paralysis, with paralytic ileus or cord-bladder, or intercostal weakness and respiratory distress; the involvement of the medulla, with difficulty in swallowing, facial palsies, paralysis of the vocal cords and of the extrinsic muscles of the eyes; or involvement of the cerebrum to produce encephalitic changes. All of these changes may occur, singly or in various combinations, to produce greatly varying pictures. Indeed, in very small children, paralysis may be the first symptom noted.

Spinal fluid changes observed in poliomyelitis are: (1) Changes in pressure, varying from normal to very high, but usually 130 to 180 mm. of water. (2) The presence of cells, varying from none to over 1,000, but usually 18 to 200 per cubic mm. Early in the course of the disease the cells often are neutrophils, and later there is a preponderance of monocytes. (3) Increase in the total protein content, usually to 60 to 80 mg. per 100 cc. but occasionally to 200 to 500 mg. per 100 cc. The sugar content is normal, but should always be determined because it is low or absent in the presence of tuberculous meningitis with which poliomyelitis is very frequently confused.

In differential diagnosis, all diseases which produce flaccid paralysis, or which cause symptoms simulating those of non-paralytic poliomyelitis, must be considered. Usually, a careful history and a period of observation will permit differentiation of these various conditions, but early in the course of the disease the differentiation may be exceedingly difficult. Tuberculous meningitis is one of the diseases most often mistaken for poliomyelitis. The low content of sugar in the spinal fluid, and later the low content of chlorides, are fairly diagnostic of tuberculous meningitis, however, and demonstration of the tubercle bacillus clinches the diagnosis.

Mumps meningitis is very common and, in the absence of parotitis, may not be distinguished from poliomyelitis except by complement-fixation or other laboratory procedures. From recent sampling, it would appear that some poliomyelitic patients, within six weeks after onset, develop complement-fixation in low titers against mumps. This phenomenon requires clarification and the study is being continued by the Los Angeles City Health Department. The reaction may be non-specific or anamnestic.

Encephalitis of other origin occurring during poliomyelitis epidemics cannot be differentiated from polioencephalitis by clinical methods. In such cases, virus and serological studies, rarely immediately available to the clinician, are required. Encephalitic involvement without some bulbar or spinal involvement must be considered rare in poliomyelitis.

In November 1949, Curnen[1] reported that a virus pathogenic for infant mice was producing in human patients in Rhode Island a disease simulating poliomyelitis with paralysis. Ten cases of this disease were observed in a group of 157 patients believed to have poliomyelitis or aseptic meningitis. (The author has been unable to diagnose any such case in the Los Angeles area.)

The Guillain-Barre syndrome, or infectious neuronitis, should not be difficult to distinguish from poliomyelitis. In infectious neuronitis there is a history of some preceding disease or infection in over 70 per cent of the cases; fever is frequently absent; many of the patients are in older age groups; the paralysis involves all extremities and sensory changes are present; there are no cells in

the spinal fluid, and the spinal fluid protein is very high, usually 500 to 1,000 mg. per 100 cc. In most cases in which, during epidemics of poliomyelitis, infectious neuronitis was diagnosed and the patient died, autopsy findings were typical of poliomyelitis. During poliomyelitis epidemics, then, a diagnosis of infectious neuronitis should be made with extreme care.

Poliomyelitis is frequently mistaken for influenza, particularly before the onset of paralysis. Observation will usually settle the diagnosis within a few days.

All told, patients with 108 different disease entities have been sent to Los Angeles County General Hospital because of suspicion of poliomyelitis, and differentiation was required. A careful history, necessary laboratory procedures, animal inoculation, x-ray studies, and observation over a suitable time interval, all may be necessary in a given case to establish the correct diagnosis or to rule out poliomyelitis.

The poliomyelitis epidemic of 1948 was the most severe ever experienced in Southern California. At that time, many changes were made in the treatment of patients who had respiratory impairment. The measures included tracheotomy, endotracheal suctioning of mucus, positive pressure air or oxygen administration, antibiotic therapy against secondary infections, and the development of an enlarged consultant staff as a team to meet the various exigencies arising from a total hospital load of 3,094 cases.

The staff of this team contained representatives of the following specialties: anesthesiology, gynecology and obstetrics, surgery, orthopedics, otolaryngology (including bronchoscopy), physiatry, urology, neurology, cardiology, neurosurgery, and biochemistry. The team also included specially instructed nurses, and a mechanical engineer. Pathologists and physiologists were frequently consulted. Electricians were immediately available 24 hours daily to act in event of power failure. A psychiatrist should have been part of the team, but none was available. This team was invaluable in shortening the time necessary to establish the correct diagnosis in puzzling cases, as well as in saving lives through improvising on-the-spot or long range treatment procedures for the various bizarre and numerous complications constantly arising.

Electrophrenic stimulation was tried and discarded as thoroughly impractical.

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Treatment of Poliomyelitis with Involvement of the Respiratory System

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SUMMARY

The mortality rate of poliomyelitis may be reduced by early measures to prevent anoxia and its subsequent complications.

Constant nursing care, early tracheotomy, the giving of oxygen, proper use of the respirator and positive pressure equipment are essential in the proper management of patients with poliomyelitis who have respiratory involvement.

THE management of the patient who has poliomyelitis and interference with respiration offers a challenge to the clinician. It is from this group of patients that the mortality rate for this disease is derived. If lives are to be saved, life-saving procedures must be instituted early in the course of the disease. Treatment must be directed toward prevention of fatal complications.

Successful management in such cases requires teamwork by experienced personnel and availability of adequate equipment and facilities. The burden of patient care rests with the nursing staff and they must be instructed in the newer approach to treatment and what they are expected to do.

Complications which most often prove fatal are prolonged anoxia, atelectasis, pulmonary edema and disturbance of blood electrolytes and serum proteins. Treatment must be such as to prevent or to correct these complications as they develop. The cause of anoxia should be determined and, if possible, corrected. Prevention of anoxia may be accomplished in many instances by the early performance of tracheotomy and use of the respirator.

Information presented herein is based on observations of more than 6,000 patients with poliomyelitis treated at the Los Angeles County General Hospital in the four-year period 1946-1949. Tracheotomy was done in 357 cases. Use of a respirator was required in 495 cases.

Indications for tracheotomy are (1) occlusion or impending occlusion of the airway due to secretional obstruction, which is aggravated by the inability of the patient to swallow, cough or maintain a free airway, and paralysis or spasm of the vocal cords; (2) massive atelectasis; (3) development of respiratory symptoms requiring a respirator, in a patient previously able to void the secretion of mucus; in such patients the intrathoracic negative pressure increases due to the partially obstructed airway, and mucus then is sucked into the lower bronchial tree, causing plugging and atelectasis; (4) persistence of cyanosis in spite of what seems to be adequate respiratory exchange; and (5) physical resistance by the patient to the aspiration of mucus from the respiratory tract.

Advantages of tracheotomy are as follows: (1) A clear airway is assured. (2) Suction and bronchoscopy may be performed easily. The cooperation of the patient for such procedures is not required. (3) Positive pressure may be readily applied for improvement of ventilation, prevention of pulmonary edema and atelectasis. (4) For many patients it has proven to be a life-saving measure.

Early tracheotomy is stressed. If the procedure is performed before any emergency sets in, bronchoscopy may be carried out, mucus or plugs removed, oxygen supplied through the bronchoscope tube and a more leisurely operation performed over the tube. This is urged in the performance of tracheotomy on all patients but particularly children. The incidence of pneumothorax and subcutaneous emphysema will be reduced.

The Bennett flow-sensitive intermittent positive pressure unit is of great value in the performance of tracheotomy on the patient who requires respiratory assistance. The patient is assured adequate ventilation throughout the entire procedure. If he is capable of initiating or maintaining his own breathing, this machine offers no interference.

A high tracheotomy is preferred. The trachea should be entered at the level of the second tracheal ring. It may be necessary to sever the isthmus of the thyroid. Bleeding should be anticipated and adequately controlled. High tracheotomy simplifies subsequent nursing care for the respirator patient. It is wise to use the largest tracheotomy tube compatible with the diameter of the trachea. However, the tube should not reach the bifurcation of the trachea.

To prevent complications due to electrolyte imbalance it is necessary to obtain blood sodium, chloride, carbon dioxide, potassium and pH determinations. The blood pH is of the utmost importance. It is the best way to distinguish between respiratory acidosis and true alkalosis. In both conditions the carbon dioxide combining power is elevated. However, if the blood pH is low the conditions should not be confused. The treatment for respiratory acidosis is improvement of ventilation.

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Gastric suction with removal of chlorides, and the injudicious use of sodium, may cause alkalosis in some cases. The treatment of this condition is the intravenous administration of ammonium chloride and normal saline.

Total proteins may be reduced and the albumin-globulin ratio often is reversed. Administration of plasma intravenously is the treatment of choice.

If the patient has some degree of interference with respiration but a respirator is not needed, the following program may prove beneficial. (The program entails 24-hour nursing care and availability at the bedside of all necessary equipment for the care of each patient.)

Oxygen, when indicated, should be administered by nasal catheter if the patient does not have a tracheotomy. If the patient is tracheotomized there should be an adapter to connect the oxygen catheter with the opening in the tracheotomy tube. This is very important in the case of small children for whom a No. 2 or No. 3 tracheotomy tube is used, because if the catheter were to be inserted into the tube, it would further occlude the airway and impair exhalation. In such circumstances pulmonary acidosis would be liable to develop. If a larger tube is used, a small catheter may be inserted into it.

Mucus may be removed from the trachea and bronchial tree by gentle suction through the tracheotomy tube. Prior to suctioning, a few drops of normal saline solution containing 200 units of penicillin per cc. may be instilled into the tracheotomy tube. The suction catheter should be small enough to pass through the tracheotomy tube without undue force. The tip of the catheter should be rounded. The tracheotomy inner tube should be removed frequently and thoroughly cleansed.

In order to facilitate drainage of mucus, the patient may be placed in a steep Trendelenburg position at regular intervals. However, constant use of this position should be avoided as the weight of the abdominal viscera against the diaphragm might further embarrass respiration and reduce cardiac output.

It is wise to pass a Levine tube at the start of treatment. Wangensteen suction apparatus should be at hand. Acute gastric distention is common, and immediate emptying of the stomach may be a life-saving measure. Vomiting, aspiration of vomitus and occlusion of the airway may occur.

Diet: Although the patient may be critically ill, if extreme care is used a formula may be fed by continuous drip through the Levine tube. The formula should be high in protein and carbohydrate, low in fat, with essential amino acids, vitamins and potassium added. At the first sign of gastric or abdominal distention, feeding should be temporarily discontinued. The diet should be a supplement to fluids, plasma and whole blood given intravenously. As the patient improves, more calories may be given either orally or by Levine tube, depending on ability to swallow.

Pain due to muscle spasm is best controlled by use of acetylsalicylic acid and hot packs. If the pain is severe, Intocostrin® (curare extract) may be used. The results are usually excellent if adequate dosage is given.

If headache persists, spinal puncture frequently gives relief, even in those patients with low spinal fluid pressure. Headache may be due to anoxia and in such cases supplemental oxygen may give prompt relief. Sedation should be avoided, particularly with drugs known to embarrass respiration.

Fever may be controlled by acetylsalicylic acid (given through the Levine tube or by rectum). When the patient is critically ill and the temperature high, hot packs should not be used. It is more important that the patient be allowed to rest than to be subjected to such a fatiguing and disturbing procedure. If there is sufficient spasm of the intercostal muscles and diaphragm to embarrass respiration, Intocostrin® and hot, light compresses should be used.

The pulse and blood pressure should be checked frequently and the patient observed for any change in respiration. A respiratory ventilation meter for the measurement of tidal ventilation has been developed recently. Frequent use of this instrument helps to determine when a respirator is indicated. However, clinical experience alone will generally enable one to determine when patients need assistance.

To combat secondary infection, penicillin in routine dosage should be given to patients who are tracheotomized or who have involvement of the muscles of respiration. If the patient is unable to void urine, catheterization should be done when necessary. In-dwelling catheters are occasionally necessary.

Abdominal distention is treated by Wangensteen suction, rectal tube, neostigmine, and hot compresses.

When the patient's condition is no longer critical a program of physical therapy should be instituted.

CARE OF THE RESPIRATOR PATIENT

If signs of anoxia develop in a patient with a clear airway, a respirator should be used. Mechanical assistance is not contraindicated in the treatment of bulbar poliomyelitis. Pulmonary edema is liable to supervene without warning if clinical cyanosis is allowed to develop. Often the first signs of anoxia are headache, increase in the pulse rate, sweating of the forehead, restlessness and anxiety. Irreparable damage to the central nervous system may be prevented if the patient is offered respiratory assistance prior to becoming irrational and semi-comatose.

Before placing the patient in a respirator, if a tracheotomy has not been performed, the advantages should be considered and a decision reached. With adequate equipment and help it may be performed later. However, to avoid emergency procedures is a step toward saving lives. The patient should be told why a respirator is necessary and instructed as to how to breathe with the machine.

NEW EQUIPMENT

To prevent complications which in the past have proved fatal to the respirator patient, new equipment was devised at the Los Angeles County General Hospital. This equipment consists of a positive pressure attachment which operates by means of a small bellows in synchronization with the respirator. When the respirator is in a negative cycle the positive pressure unit is in a positive cycle. Air is forced under pressure through the tracheotomy tube.

This is important in overcoming the increase in intrathoracic negative pressure due to the partially occluded airway. Better ventilation is obtained. Because of the action of the expiratory valve the patient is not required to breathe out against any resistance other than that offered by the tracheotomy tube. Respiratory acidosis, atelectasis and pulmonary edema are reduced to a minimum. Air, oxygen or oxygen and helium may be administered directly into the unit. Humidification of the gases is important. There is an air filter to reduce the hazard of infection of the trachea due to contaminated room air.

In order to improve the respiratory pattern of the respirator, a cam was developed. The cam makes possible a slow, uniform inspiratory pressure rise and a rapid expiratory flow simulating the pattern of normal respiration. Chest pain presumably due to an increase in intrathoracic negative pressure has been eliminated. Adequate ventilation can be obtained with lower pressure settings than were used previously. Thus, tidal ventilation is increased by combination of the positive pressure unit and the cam. The equipment is a valuable adjunct to the management of the tracheotomized patient who requires a respirator. It should be employed as soon as the patient is in the respirator. Its use allows time to make all the necessary adjustments without undue haste.

If the patient is unable to synchronize with the respirator, hot packs should be placed against the chest and Intocostrin® should be given. Several doses of the drug may be required. If the patient's inability to synchronize with the respirator is due to pulmonary acidosis, positive pressure will correct this incompatibility.

As soon as the patient is adapted to the respirator, routine procedures may be carried out. It is important that pressure points be well padded. The collar should not cause the patient any discomfort and it should be pushed well into the respirator by a metal shield to allow adequate room for the care of the tracheotomy tube.

During the first few days in the respirator, most attention should be directed toward keeping the patient alive. Care of the patient's body should be reduced to a minimum. To keep the airway free, removal of mucus may require the full attention of a nurse. If the patient is to be saved it becomes a matter of 24-hour nursing care, properly functioning equipment, and fluid balance.

A common error is neglecting to remove mucus from the main bronchi by suction. A clear upper airway does not mean that the main bronchi are free of mucus. Accumulation of mucus leads to anoxia and its complications. Nurses must understand the importance of maintaining a free airway. If cyanosis persists after proper suctioning, bronchoscopy should be performed.

Rules governing the feeding of the non-respirator patient apply equally well to the patient in a respirator. Gastric distention is more common and it is often necessary to use Wangensteen suction. However, the importance of maintaining normal protein values is well established and it is advisable to feed the critically ill patient. When food is offered by mouth, the diet should be appetizing, non gas-forming and highly nutritious. The difficulty connected with swallowing due to the action of the respirator requires that adequate time be allowed to feed the patient properly.

Plasma, whole blood and other fluids should be given as indicated. It is important to carry out blood chemistry determinations at regular intervals. Blood pressure should be checked frequently. Periodic x-ray films of the chest blood cell count, urinalysis and culture of blood should be obtained periodically. If positive pressure is available the purely mechanical difficulty of obtaining the specimens is reduced to a minimum.

Mechanical accidents occur. The best safeguard is to know what might happen and to take steps to prevent it. By far the most common accident is a leak at the collar, permitting the respirator pressure to fall. Respirator ports may be left open, or they may work loose. A reliable warning device connected with the respirator is desirable. If positive pressure is being used, death may be avoided but such an accident always causes the patient considerable anxiety and increases the demands made on the nursing staff.

The patient may need *constant* supplemental oxygen. Oxygen tanks should not be permitted to become empty. The oxygen gauge should be turned toward the nurse.

Suction machines should be in good working order. An adequate supply of suction catheters should be at hand, as they are easily contaminated.

It is important to change the tracheotomy tube at frequent intervals. However, it should not be removed during the first 24 to 36 hours. It may be exceedingly difficult to replace before a track is established.

The speed of the respirator must be watched. The ideal speed is that which assures the patient adequate ventilation without producing hyperventilation syndrome. With positive pressure and the cam, adequate tidal air is obtained at fairly low pressure settings. The proper pressure may be determined by frequent use of the respiratory ventilation meter. A tidal ventilation of 400 to 600 cc. is adequate.

To aid in drainage of mucus, the respirator may be tilted. However, the Trendelenburg position must not be used over a prolonged period. When the position of the respirator is changed, examination

for possible pressure leaks should be made. It is important that the patient's collar does not impede circulation.

In order to withdraw the patient from the respirator and to carry out proper nursing procedures, positive pressure equipment should be used to maintain adequate ventilation. This equipment also permits packing the patient and starting physical therapy at an early date.

There are many complications common to the respirator patient which require early detection and careful management. Pneumonia and infections of the urinary tract are common. Treatment depends upon the causative organism. Decubitus ulcers are a problem. Air mattresses, frequent changing of the patient's position and maintenance of normal protein values are of help. Sinusitis may develop due to the disturbance of the nasal passages by frequent suction and the presence of a Levine tube. This condition may be reduced to a minimum by frequent changing of the tube, nasal shrinkage and topical application of antibiotics. Infections of the trachea secondary to tracheotomy and trauma, due to suction catheters, are frequent. A common offender is Pseudomonas aeruginosa. The most efficacious treatment has proven to be sulfonamides and streptomycin. Bacteremia due to the previously mentioned organism and occasionally E. coli, may occur. Streptomycin, aureomycin and chloramphenicol are the drugs of choice in the treatment of this complication. Hypertension may develop, the cause of which is usually obscure. Psychiatric problems arise. It is urged that a psychiatrist be in attendance to direct proper treatment.

Every encouragement possible is given the patient. Immediate members of the family are constantly warned against doing or saying anything which might conceivably upset the patient. Morale is an important factor in recovery.

A sincere attempt should be made to segregate the new, acutely ill patient from others who have the first few days of their illness behind them. The possibility of secondary respiratory infection must be guarded against. Penicillin should be used routinely in adequate dosage.

Patients should be removed from the respirator as soon as possible. However, it is a mistake to attempt to remove a patient from a respirator if the respiratory exchange is inadequate. This leads to disaster. By frequent use of the respiratory ventilation meter this error may be avoided.

The rocking bed, which is relatively new in the treatment of poliomyelitis, will undoubtedly contribute to satisfactory early removal of patients from the respirator. However, experience gained by limited use of this equipment indicates that care should be taken that the patient has adequate ventilation before the bed is used. It may give the necessary assistance to borderline patients and permit good physical therapy at an early date. Perhaps the rocking bed will be the answer to the so-called respirator-fast patient. Experience will determine the answer.

Before attempt is made to remove the tracheotomy tube, the patient should be able to get along without supplemental oxygen. If this is accomplished over a period of days, a small tracheotomy tube may be substituted for the larger one and be closed off. If, in a matter of two or three weeks, the patient has not required suctioning through the tracheotomy tube, it may be removed. Positive pressure may be administered by mask in order to continue adequate nursing care and physical therapy. If a condition arises which impairs the patient's ventilation, another tracheotomy should be carried out without hesitation.

In the management of the respirator patient, it is extremely important that physicians and nurses secure the patient's confidence.

Alterations in Serum Protein Levels in Acute Human Poliomyelitis: Rationale for Therapy

JACK SHELDON CHUDNOFF, M.D., *Los Angeles*

SUMMARY

Serial determinations of serum protein levels in acute human poliomyelitis revealed a progressive drop of the serum albumin level which bore close relationship to the amount of clinical paralysis. This loss of serum albumin began about the third day after onset of clinical symptoms and progressed to the tenth day or longer. The more severe the clinical involvement, the less was the tendency to spontaneous correction of the albumin deficiency. Declining serum albumin levels were concomitant with progressively rising serum globulin values.

When pooled irradiated human blood plasma was administered, the depleted serum albumin levels were stabilized or made to approach normal, depending upon the severity of clinical involvement. It is felt that the administration of blood plasma resulted in definite clinical benefit with regard to the severity, extent, and duration of paralysis.

SPORADIC reports in medical literature have attributed beneficial results to the administration of whole blood serum or plasma[3, 4, 5] in acute human poliomyelitis. Other reports have stated that no apparent benefit results from administering large amounts of gamma globulin,[1] in spite of experimental evidence that strains from the three recognized types of poliomyelitis virus are agglutinated experimentally very readily by gamma globulin derived from pooled human plasma.[2] No specific rationale has been advanced to justify therapy with blood plasma. Although use of plasma was on an empiric basis, the results in a few reported instances were described as dramatic. For that reason and because of other studies soon to be reported, systematic investigations of the blood electrolytes and serum protein levels in acute cases of human poliomyelitis were made during the epidemic of 1948 which occurred in Los Angeles County. During the epidemic, 3,165 cases were reported and 3,094 of the patients were admitted to the Los Angeles County General Hospital. The impact of such a case load of this crippling disease provided impetus to reexplore old therapeutic possibilities and to search for new.

Pilot observations of the serum protein levels in a group of 40 consecutive patients, all severely ill and all confined to respirators, revealed unexpected and startling alterations from normal. During the time these striking protein changes became apparent in the laboratory, gross peripheral edema also was evident in many of these patients. There was no apparent reason for the appearance of the edema. The period during which nutrition had been withheld was too brief for edema to have resulted, and the volume of parenteral fluids was insufficient to have contributed to edema. Obviously, further investigation into the entire subject of serum protein levels, especially albumin fractions, was imperative.

The correlation between low serum albumin and peripheral edema has long been established and accepted in cirrhosis of the liver, nephrosis, and other clinical diseases. A question that arises, then, is: If peripheral edema occurs — and peripheral edema was present in many of the patients observed — is it not feasible for interstitial edema to occur within the central nervous system and contribute to the paralysis? It has been observed frequently in this disease that the onset of paralysis occurs suddenly and extensively; also that its disappearance may follow the same variable course without adequate explanation: The nerves do not function but could not have been destroyed.

In order to explore the patterns of serum protein changes, it was decided to determine serum protein levels with albumin-globulin fractions in cases of graded severity. For this purpose, all cases in this study were empirically classified into three categories:

I. *Mild*—Cases of non-paralytic poliomyelitis, or cases in which there was paresis or paralysis totaling less than one-third of the body musculature. No cases of bulbar involvement were included.

II. *Moderate*—Cases in which there was paresis or paralysis of more than one-third of the total body musculature. Bulbar involvement was not excluded if the use of a respirator was not required.

III. *Severe*—Cases in which there was paresis or paralysis of more than one-third of the body musculature. Patients in this classification all had respiratory muscle or bulbar involvement, had had tracheotomy, and were in respirators.

Presented as part of a Symposium on Recent Advances in Knowledge and Care of Patients with Bulbar and Respiratory Poliomyelitis before a Joint Meeting of the Sections on Pediatrics and Public Health at the 79th Annual Meeting of the California Medical Association, San Diego, April 30-May 3, 1950.

The study here reported was aided by grants from the College of Medical Evangelists and from the National Foundation for Infantile Paralysis.

No equivocal cases were accepted for this study. It was not necessary to include borderline or transitional cases which could not be fitted into the three categories.

TABLE 1.—*Clinical Severity of Cases Studied: 75 Cases*

	Mild	Moderate	Severe
47 cases (Controls—conventional treatment only)	25	13	9
28 cases (Treated—conventional treatment plus plasma)	4	9	15

In each case studied serum protein levels and albumin-globulin fractions were determined daily for five days from the date of admission to the hospital. The day of admission to the hospital invariably was the day on which the case was accepted in this study. Following these initial determinations, levels were determined every second day for an additional five determinations; and if the patient remained in the hospital, levels were determined every third day thereafter. For those patients who were to be treated, levels were determined daily until the day of treatment, and on each treatment day the levels were determined before blood plasma was administered. At the termination of plasma treatment, invariably five consecutive days, levels were determined as before, every two days for five determinations, and every three days thereafter until the patient was discharged from the hospital. The plasma used for treatment in this study was pooled, irradiated human blood plasma, given in a dosage of 5 cc. per pound of body weight daily, for a minimum consecutive period of five days. With few exceptions, no more than 1,000 cc. of plasma was given to a patient on any single day.

It should be stated that all patients observed during this epidemic were given routine care and treatment. No specific measures were used either in diagnosis or treatment that would differ materially from the routine care given elsewhere to patients with acute poliomyelitis. Upon institution of this study, consecutive cases were accepted into the series, classified, and the patients observed closely in the manner described. In alternate cases, with few exceptions, in addition to the usual measures employed at this hospital, pooled, irradiated human plasma was given intravenously in the manner related. For purposes of description in this study, the cases in which plasma was given are considered "Treated" cases, as contrasted to the alternate paired cases of comparative severity in which plasma was not given and which are regarded as "Controls." "Treatment," as here used, means administration of plasma according to the previously stated schedule.

All laboratory determinations were performed in a research laboratory organized specifically for this project. Blood samples in which hemolysis was noted were discarded and new samples obtained. The serum proteins were separated by Howe's sodium sulfate method[6] and measured by the biuret method of Kingsley.[7] By this method the alpha globulin fraction is thrown down with the albumin. The computed error by which the albumin fractions are thus increased over true values ranges from 20 per cent to 35 per cent, or from 0.75 gm. to 1.25 gm. per 100 cc. It was technically not feasible to correct the values for this error; the albumin values in these protocols are therefore significantly above true value, especially since in this disease the globulin is shown to be elevated.

Almost without exception, about the third day of clinical illness, regardless of the severity of involvement, there was a progressive decline in the serum albumin in direct proportion to the severity of the paralysis. This decline, which began about the third day, tended to reach its greatest subnormal value by the tenth day. Subsequent clinical relapses in severe cases were again mirrored in a decline in albumin levels from the previous level. At the same time that albumin levels declined, the serum globulin values rose in direct proportion to the severity of the clinical involvement and continued to rise far into convalescence.

In the cases of mild involvement, the serum albumin levels tended to return to normal spontaneously, a trend evident by the tenth day. In cases of moderate involvement, the drop reached its maximum by the tenth day and showed a tendency gradually to return to normal, but the level did not reach a normal for some time; in fact, at the end of three to four weeks of observation in the cases that were followed for that length of time, levels had not yet attained normal. In the severe cases, albumin depression was most severe by the tenth day of illness and showed little or no tendency to revert toward normal. In some severe cases followed for periods of 60 to 90 days, serum albumin levels still were low at the end of that time. In the event of clinical relapse, or extension of paralysis, the partial stabilization at a subnormal level that had occurred was disrupted and further reductions took place. Albumin-globulin ratio reversal was common.

Because of the usual delay in diagnosis and in the hospitalization of patients after the onset of symptoms, treatment was not initiated before the dropping serum albumin level became evident. As a rule, treatment was initiated as soon as possible after the case was accepted for this series.

In the *mild* cases, it was found to be possible not only to halt the decline in albumin level, but actually to raise the level above normal. Probably in most such cases, treatment would not be indicated. In those treated, the patient appeared able to maintain the serum protein levels at or near normal values, and clinical progression of paralysis was arrested or even regressed.

In the *moderate* category, it was possible to stabilize the serum albumin level at whatever level was found present at the onset of therapy. At times it was possible to raise the albumin level to normal, but as a rule it remained slightly subnormal. After therapy was terminated, subnormal albumin levels

persisted for many weeks. There appeared to be little or no intrinsic ability to sustain an artificially elevated albumin level.

In the *severe* class, the maximum benefit obtained from the schedule of therapy used was the temporary stabilization of the dropping serum albumin level. There was little significant tendency shown for it to revert toward normal, and virtually no evidence to indicate that patients could retain the temporary benefit of replacement. When therapy was stopped, the tendency was for the albumin level to resume the decline progressively over an unpredictable period of time (see Charts 1, 2, 3, and 4).

CLINICAL IMPLICATIONS

At the time each case was accepted for this study, each patient was seen by the same staff member* and assigned to one of two well trained physical therapists for complete grading of muscle function. The same technician repeated the muscle grading on the third, seventh, 14th and 21st hospital days. Because of the desire to keep evaluations unbiased, the therapists were not indoctrinated into this program.

The value of plasma therapy is debatable in the mild cases. In those cases the patients appeared to do equally well with or without therapy. The ability to produce serum albumin levels greater than normal is of questionable value. In this report only typical cases were included, and in this discussion no consideration is being given to those patients in whom poliomyelitis progressed from mild to severe. That such progression does occur, however, provides a basis for argument for protein therapy in all cases.

The number of *mild* cases treated was small, for several reasons: (a) the consistency of the favorable response, as indicated by laboratory tests, to the

*John Affeldt, M.D., senior resident, Communicable Disease Unit, Los Angeles County General Hospital.

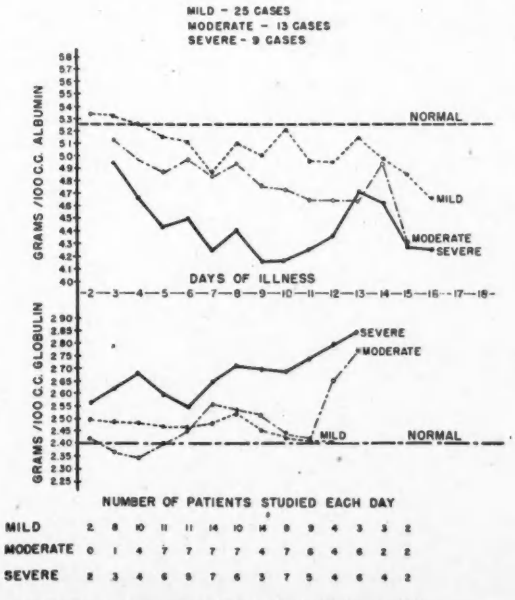
MILD - 25 CASES
MODERATE - 13 CASES
SEVERE - 9 CASES
GRAMS /100 C.C. ALBUMIN
NORMAL
MILD
MODERATE
SEVERE
DAYS OF ILLNESS
GRAMS /100 C.C. GLOBULIN
SEVERE
MODERATE
MILD
NORMAL
NUMBER OF PATIENTS STUDIED EACH DAY
MILD 2 8 10 11 11 14 10 14 8 9 4 3 3 2
MODERATE 0 1 4 7 7 7 7 4 7 6 4 6 2 2
SEVERE 2 3 4 6 5 7 6 3 7 5 4 6 4 2

Chart 1.—Serum Protein Levels in Poliomyelitis.

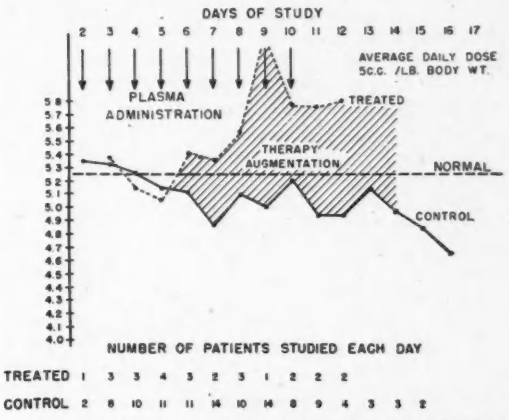
DAYS OF STUDY
AVERAGE DAILY DOSE 5c.c. /LB. BODY WT.
PLASMA ADMINISTRATION
TREATED
THERAPY AUGMENTATION
NORMAL
CONTROL
NUMBER OF PATIENTS STUDIED EACH DAY
TREATED 1 3 3 4 3 2 3 1 2 2 2
CONTROL 2 8 10 11 11 14 10 14 8 9 4 3 3 2

Chart 2.—Serum Albumin Levels in "Mild" Poliomyelitis.

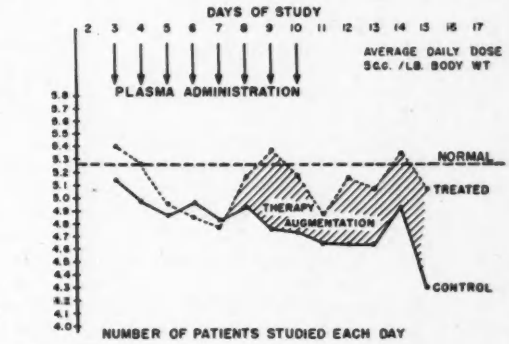
DAYS OF STUDY
AVERAGE DAILY DOSE 5c.c. /LB. BODY WT
PLASMA ADMINISTRATION
NORMAL
TREATED
THERAPY AUGMENTATION
CONTROL
NUMBER OF PATIENTS STUDIED EACH DAY
TREATED 2 8 7 6 5 7 5 7 4 4 2 4 3
CONTROL 0 1 4 7 7 7 7 4 7 6 4 6 2 2

Chart 3.—Serum Albumin Levels in "Moderate" Poliomyelitis.

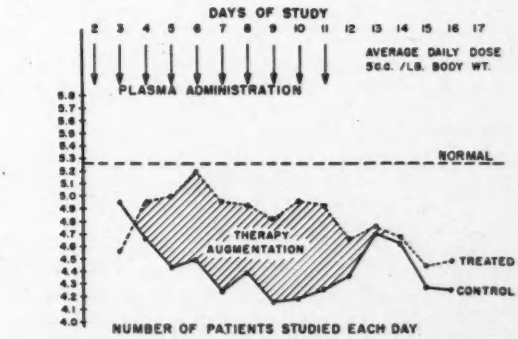
DAYS OF STUDY
AVERAGE DAILY DOSE 5c.c. /LB. BODY WT.
PLASMA ADMINISTRATION
NORMAL
THERAPY AUGMENTATION
TREATED
CONTROL
NUMBER OF PATIENTS STUDIED EACH DAY
TREATED 2 4 9 10 10 13 10 13 6 7 5 5 5 5
CONTROL 2 3 4 6 5 7 6 3 7 5 4 6 4 2

Chart 4.—Serum Albumin Levels in "Severe" Poliomyelitis.

albumin levels; (b) the greater burden of more severely ill patients in *moderate* and *severe* category; and (c) the limitation of supplies of irradiated plasma for this study. Within the small series of treated cases there were no instances of progression observed. On the other hand, in the control series there were repeated instances in which *mild* cases progressed to a more severe category and in which plasma was then given with benefit. These cases, however, were dropped from the series because they did not lend themselves readily to inclusion in this report. When a sufficient number of such instances have been observed and analyzed, future reports will be submitted if data warrant.

In the *moderate* cases, protein therapy produced notable diminution of toxicity. In addition, completed protocols, including the muscle grading charts, warrant the opinion that replacement therapy is of definite value. The dosage of 5 cc. per pound of body weight every 24 hours is probably adequate, but should be carried on longer than five days. It probably should be continued until such time as the laboratory tests reveal a reversion of the serum albumin level to normal over a period of several days.

It is felt that the greatest benefit of protein therapy was to patients in the *severe* category, despite the impression that the dosage used was inadequate and the period of therapy not long enough. Observations made subsequently revealed that larger doses of plasma than those used in this study could not return the serum albumin level to normal. The latter studies were not amplified, but indicated that in the catabolic phases of the illness the replacement therapy was of appreciable benefit: There was a definite diminution of toxemia and an appreciable stabilization, albeit temporary, of the progression of paralysis. There were repeated instances of comatose patients returning to consciousness with plasma therapy, only to relapse after therapy was terminated.

To attain maximum benefit, plasma therapy should be instituted as soon as possible. It was not unusual in the control series, especially in the *severe* category, for relapse to follow temporary clinical stabilization. Because of the critical status of these patients plasma therapy was instituted according to this schedule. Its benefits were easily apparent, but were probably not as efficacious as they might have been if therapy had been instituted earlier. There are no available criteria as yet to prognosticate relapse. The severity of relapse, on the other hand, is well mirrored by falling albumin levels.

DISCUSSION

The authors are aware of the danger of drawing conclusions from a small series of cases. That poliomyelitis is a disease both protean and variable in its manifestation and course is well appreciated, especially since there are no coldly objective criteria of improvement which are not duplicated spontaneously regardless of therapy. Nevertheless, based upon the clinical observation of over 6,000 cases of acute human poliomyelitis in four years, it is felt that an expression of opinion is warranted.

The startling consistency with which depleted serum albumin levels occur in acute human poliomyelitis is a significant contribution to the litera-

TABLE 2.—*Albumin and Globulin Values by Serial Days in Three Patients with Severe Poliomyelitis*

Normal Values: Serum albumin—5.26 grams/100 cc.
Serum globulin—2.31 grams/100 cc.

CASE 1

Days of Illness	Albumin grams/100cc.	Globulin grams/100cc.
13	3.09	3.42
15	2.58	2.95
19	2.71	2.66
23	3.11	3.34
26	3.18	3.41
(Patient relapsed—Condition critical—Plasma given as indicated by symbol Pl.)		
27	3.55	3.61—Pl.
28	3.66	3.75—Pl.
29	....	....—Pl.
30	4.66	3.51—Pl.
31	4.02	3.41
33	3.80	3.00
(Patient unable to maintain levels)		
37	3.80	3.17
40	3.69	3.05
50	4.11	3.00
55	3.73	2.97
60	3.95	2.97
74	4.11	2.93
(Patient lived—Maximum paralysis—Transferred out of hospital in respirator)		

CASE 2

Days of Illness	Albumin grams/100cc.	Globulin grams/100cc.
4	5.04	2.98
5	4.22	2.64
7	4.11	2.12
8	4.38	2.53
10	4.56	2.83
12	4.20	2.76
14	3.66	3.24
(Died on fifteenth day—No treatment)		

CASE 3

Days of Illness	Albumin grams/100cc.	Globulin grams/100cc.
5	4.24	3.24
6	3.98	3.10
7	4.13	3.07
8	4.06	2.63
9	3.18	3.24
(Reversal of ratio)		
10	3.57	3.32
11	4.13	2.44
12	4.15	2.53
13	4.08	2.48
21	4.40	2.85
39	4.20	2.46
59	4.66	2.63
67	4.75	2.32
(Patient lived—No treatment)		

TABLE 3—*Magnitude of Serum Albumin Loss in "Severe" Cases*

Patient	Amount of Serum Albumin Reduction per 100 cc. Serum
1	.5 grams/24 hours
2	.2 grams/24 hours
3	.7 grams/72 hours
4	1.0 grams/72 hours
5	1.1 grams/72 hours
6	.8 grams/72 hours
7	1.0 grams/72 hours
8	2.1 grams/ 6 days
9	1.3 grams/ 4 days
10	1.0 grams/ 2 days
11	1.7 grams/14 days
12	2.3 grams/14 days
13	1.4 grams/ 4 days
14	1.7 grams/10 days

ture and knowledge concerning poliomyelitis, which up to the present time has not been publicized. That this depletion of serum proteins occurs in linear relationship to the severity of paralysis appears to be highly significant. Serum albumin levels of equal magnitude are accepted without dispute as the cause for peripheral edema in other clinical entities. The effects of transfusion of immune bodies in the plasma utilized can be reasonably discounted from the work of Bahlke and co-workers in 1945.[1] The study being presented represents the first known attack therapeutically on a hitherto undescribed physiologic deficiency occurring in human poliomyelitis.

In addition to the data presented here, serum albumin patterns have now been followed in approximately 150 cases (more than 1,600 determinations having been made) and these are consistent in all details with those in the series reported. It remains for others to repeat and substantiate this work in an attempt to crystallize thinking on the benefits which are felt to accrue from the administration of pooled, irradiated human blood plasma in adequate amounts to patients with early poliomyelitis over a sufficiently long period.

It can be stated with assurance that in the *mild* and *moderate* categories not only did results of laboratory tests confirm benefits from administration of plasma, but in no case in the series in which

TABLE 4.—*Estimate of Clinical Results from "Muscle-Grade" Charts Plus General Clinical Evaluation. (Observations from the Third to the Fourteenth Hospital Days.)*

Category	No. of Cases	Stationary	Progressing	Improved
Mild—not treated	25	17	6	2 (8%)
Treated	4	2	1	1 (25%)
Moderate—not treated	13	8	4	1 (9%)
Treated	9	4	3	1 (23%)
Severe—not treated	9	0	8	1 (10%)
Treated	15	3	8	4 (27%)

plasma was given early was there clinical progression into a more severe category. Observations within the *severe* group are more controversial, for reasons previously stated. Table 2 presents data that are interpreted as evidence of both laboratory and clinical benefit following treatment as outlined.

It is the primary purpose of this report to describe the acute changes in serum protein levels in human poliomyelitis. These changes have not previously been reported. Secondarily, it is desired to elucidate a rationale for treatment with plasma as well as to report observations in a limited series with such treatment (Tables 2, 3, and 4).

6333 Wilshire Boulevard.

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Biochemical Alterations in Acute Human Poliomyelitis: Electrolyte Patterns and Trends

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SUMMARY

Pronounced alterations occur in the biochemical findings in acute poliomyelitis. These are derived from three major mechanisms: (a) inefficient pulmonary gaseous exchange, resulting in respiratory acidosis; (b) profound changes in nitrogen metabolism, resulting in decreased serum albumin, tissue destruction, and increased urinary nitrogen; (c) losses of electrolytes through extrarenal channels such as lung and tracheal secretions, sweating, and gastrointestinal disturbances.

The extent of these alterations may be defined by appropriate serum and urinary biochemical determinations. These determinations are valuable both from a therapeutic and a prognostic standpoint. They also contribute to further understanding of physiologic and pathologic conditions in acute poliomyelitis.

AS the possibility of major blood chemistry alterations in an acute infectious disease such as poliomyelitis is obvious, it is singular that few studies have been made in that field until recently.

Recent experience indicates that such changes may be of primary importance in determining the progress of the patient. In many cases, fatal termination of the illness is due largely to changes in blood electrolytes that are incompatible with continued life.

The poliomyelitis epidemic of 1948 in Los Angeles County afforded ample opportunity to observe and study these changes. The following table presents in summary some factual data with reference to the epidemic and the relation of this study to it.

As may be seen from Table 1, the 1948 epidemic produced an unusually large number of severely ill patients requiring respirator treatment. This intense case load emphasized the problems of clinical management, and stressed the lack of available information relative to altered physiologic states and biochemistry in this disease. For example, why did many patients confined to respirators become bloated, cyanotic, encephalitic and fail rapidly in spite of all known therapeutic efforts?

In order to provide answers to these questions, special laboratory facilities were set up as rapidly as possible, and a series of studies initiated. The objectives of these studies were to determine whether changes in electrolytes occurred during the progress of the disease which could be of diagnostic, prognostic or therapeutic value.

This report describes the general plan and findings, particularly with respect to acid-base balance. It also indicates the usefulness of the various biochemical determinations utilized, particularly with regard to the clinical management of patients acutely ill with poliomyelitis.

There are three major factors which, particularly in respirator patients, may be effective in producing these extensive electrolyte changes in body fluids.

First, the control of the extent and frequency of breathing has been transferred from the natural respiratory center to a mechanical one—the respirator. This means the possibility for major shifts in acid-base balance, plasma pH, and alkali reserve.

Secondly, in common with many other acute illnesses, a profound alteration in protein metabolism occurs very promptly, indicated by increased nitrogen excretion, decrease in serum albumin, and considerable tendency toward edema.

Third, because of extensive tissue destruction, the difficulties of maintaining adequate electrolyte intake without aggravating edema, and sometimes kidney and heart failure, pronounced imbalance may occur in the distribution of the principal electrolytes, sodium, potassium, chloride, bicarbonate, etc., in the serum and extracellular fluid.

Other phases of these studies have already been reported[1, 2, 8] or reports are in process of preparation.

Procedure: The patients in this study had all been admitted to the Communicable Disease Unit of the

TABLE 1.—*General Summary and Classification of Poliomyelitis Cases, 1948 Epidemic*

	Cases
Total (Los Angeles County)	3,165
Total at Los Angeles County General Hospital	3,094
Bulbar, bulbospinal and upper cervical involvement	603
Mortality rate among the 603	19.4%
Respirator required	294 (peak load 82)
Tracheotomies	354
Cases with blood chemistry studies	148
(a) Blood electrolytes	60
(b) Plasma protein studies	88

From the Communicable Disease Unit of the Los Angeles County General Hospital and the Department of Medicine of the College of Medical Evangelists.

Presented as part of a Symposium on Recent Advances in Knowledge and Care of Patients with Bulbar and Respiratory Poliomyelitis before a Joint Meeting of the Sections on Pediatrics and Public Health at the 79th Annual Meeting of the California Medical Association, San Diego, April 30-May 3, 1950.

TABLE 2.—*Type and Frequency of Chemical Determinations*

BLOOD DETERMINATIONS	Number
Plasma pH	355
Plasma bicarbonate	379
Plasma chloride	361
Sodium	296
Potassium	296
Calcium	42
Proteins (albumin and globulin)	2,142
Miscellaneous	208
Total	4,079

URINE	Number
pH	86
Chloride	553
Sodium	328
Potassium	328
Total nitrogen	454
Total	1,749

Los Angeles County General Hospital following a complete examination in the admitting rooms, including general physical examination, neurological survey, muscle check when indicated, complete blood cell counts, urinalysis and spinal puncture and analysis. All patients in this study fulfilled the usually accepted criteria for the diagnosis of poliomyelitis.

The treatment was that routinely used in this hospital for patients with respiratory embarrassment. The method of treatment was not altered in any way before the studies were made. Such changes as were made were not put into effect until after the determinations gave specific indication as to what changes were advisable.

As far as possible the initial chemical determinations were done at once in those cases in which the patient had to be put into a respirator, and serial determinations were made at 48-hour intervals during the period of critical illness, with less frequent measurements later until termination of the hospital stay.

Due to the tremendous case load and the limitations of the laboratory personnel and facilities, many patients suitable for the study could not be included and all the determinations originally planned for each patient could not be carried out.

ACID-BASE BALANCE

The first of the biochemical problems to receive attention was acid-base balance. Clinical observation, supplemented by preliminary laboratory work, disclosed major alterations in some cases, as shown by abnormally high bicarbonate content of the serum in the presence of a neutral or acid urinary output.

To determine the nature of this shift, laboratory determinations required were serum pH, bicarbonate content, sodium, potassium, and chloride levels. In the first series of 27 patients studied, with about 125 series of chemical determinations, three-fourths of the cases showed one or more pH values below the normal limits of 7.33 to 7.45, and in several cases values were 7.05 to 7.10.

These findings were contrary to previously held ideas, that alkalosis and hyperventilation were usually found with respirator patients.

The relationships between pH, free carbon dioxide or carbonic acid, and bicarbonate concentrations which occur in various acid-base balance disturbances have been presented in graphical form by Gamble.[6]

The pH of the serum is determined by the ratio of free carbonic acid to total bicarbonate, the normal value of the ratio being about 1:12. The free carbonic acid concentration is determined by the rate at which it diffuses into the alveolar air, an inexhaustible supply being produced continually by the normal metabolic process. Any obstruction, such as decreased volume or rate of respiration, impediment to expiration or free gaseous exchange, tracheal plugs of mucous atelectasis, or edema of the lungs, which interferes with this diffusion process will cause an increased concentration of carbonic acid in the blood and consequent acidosis. The first change involves pH only and may take place in a relatively short time. If this acidosis persists for a few hours, then the renal mechanisms for pH regulation come into play, and a retention of bicarbonate occurs, with a corresponding excretion of chloride. This tends to compensate the pH changes by returning the ratio of free carbonic acid to serum bicarbonate toward normal. Fully developed respiratory acidosis involves three alterations, namely, a decreased pH, a high bicarbonate concentration, and a low chloride level.

Table 3 shows results for two series of patients for which quite complete data are available.

About one month elapsed between the two series of determinations. Although respiratory acidosis occurred in both series, it was a much more prominent finding in the first. Probable reasons for this difference between the two series are of great interest. Undoubtedly, several factors were involved in this change. During this period, intensive studies on the

TABLE 3.—*Frequency of Respiratory Acidosis in Respirator Patients*

	Series A Sept. 9 to Oct. 20	Series B Dec. 1 to Feb. 20
Number of cases	27	33
Number of blood pH determinations	125	230
Number of pH values below normal	45	15
Number of cases with one or more pH values below normal	20 (75%)	8 (25%)
Number of cases with pH below normal and high bicarbonate levels	10	3
Average of pH values below normal	7.25	7.30
Range of pH values below normal	7.05-7.32	7.25-7.32

mechanical design of the respirator were carried on, and the use of positive pressure and a modified cam was begun.[2] This use of positive pressure in particular had a very distinct effect on the incidence of lung edema. A second factor was the use of plasma protein in quantities of 400 cc. to 1,000 cc. per day for a five-day period for many of the patients in the second series. This, as has been reported[1] tended to prevent the drop in the albumin-globulin ratio, and again was influential in reducing lung edema.

Previously, in the diagnosis of acidosis or alkalosis the direct determination of blood pH was used very seldom, the condition being inferred from the carbon dioxide combining power supplemented by urine pH measurements. In respiratory acidosis, however, the acidity is caused by retention of carbon dioxide, later accompanied by high serum bicarbonate levels and a compensatory drop in chloride concentration.

Accordingly, the degree of respiratory acidosis or alkalosis can only be determined by actual measurement of blood pH, either directly or by calculation from analyses of alveolar air. Commercial apparatus for accurate measurement of pH by glass electrodes is widely available and is standard laboratory equipment, but because of the very limited experience for clinical use, it has not been generally appreciated that there is a large temperature factor in this measurement, and that accordingly measurements should be made at body temperature or 37° C.[7] Since commercial electrode equipment is not easily adapted to temperature regulation, with the aid of National Technical Laboratories, a specially designed electrode system was made up which can be immersed in a water bath and which permits anaerobic handling of the blood specimen while measurement is made. With the use of this equipment, accurate pH determination of the plasma was readily made, and the true state of the acid-base balance established.

It should be noted particularly that where obstacles to free exhalation exist, it may be easier to supply oxygen to combat anoxia than to prevent carbonic acid acidosis due to atelectasis, mucous plugging, pulmonary edema, pneumonia, etc. The concentration of oxygen supplied to the patient in the respirator may be several times that of the air, but the regulation of carbonic acid concentration is determined by the total volume of gas exchange and by the conditions under which carbon dioxide may be transferred from the capillaries of the lung to the air in the alveolar spaces.

The frequency of occurrence of excessive hypopharyngeal and tracheal secretions, atelectasis, pulmonary edema and pneumonia is especially noteworthy. In those cases in which autopsy was performed, edema of the lungs was frequently noted, and the other conditions mentioned were observed hardly less often. The volume of tracheal secretions removed by suction was large in many cases—frequently two liters or more in 24 hours. In a few instances the quantity of sodium chloride lost by this route was measured and was found to be a very significant part of the total daily loss.

TABLE 4.—*Comparison of Chloride Losses in Tracheal Washings with Urinary Excretion*

		Tracheal Washings		Urinary Excretion	
Patient	Date	24 Hr. Volume cc.	Chloride Content as NaCl (grams)	24 Hr. Volume cc.	Chloride Content as NaCl (grams)
1.	9- 9-48	2260	1.93	1660	2.2
	9-10-48	1640	1.25	1175	0.51
		Died 9-11-48			
2.	9- 9-48	1420	.74	1950	0.80
	9-10-48	1660	1.06	2460	6.15
	9-11-48	1600	1.10	700	1.19
	9-12-48	2300	1.80	1020	1.32
	9-13-48	680	.50	1530	2.75

Examples of the extent of this loss and comparison of it with losses by urinary excretion are shown in Table 4.

To determine the primary cause of this lung edema was one objective of the study, and it is no doubt due, at least in part, to the extensive changes in the blood and protein pattern. As has already been reported in a separate phase of these studies[1]—beginning about the third day of illness, a major change in nitrogen metabolism occurs, manifested by a sharp drop in serum albumin, a gradual rise in the globulin fractions, and a large increase in urinary nitrogen.

The extent of the changes in albumin and globulin concentrations was such as to produce a ratio (albumin to globulin) of less than one in a number of cases, and in general paralleled the severity of the disease.

These plasma protein changes undoubtedly play a significant part in causing lung edema, and to the extent to which they can be prevented, the problem of respiratory acidosis is minimized.

If extensive paralysis occurs, the large increase in urinary nitrogen excretion is due mainly to destruction of muscle tissue. This is apparent also in the increased potassium excretion during this phase, since the intracellular mineral constituent is primarily potassium. If kidney failure does not occur, the findings may be a normal serum potassium level, combined with a negative potassium balance.

At a later stage, if recovery and tissue regeneration are present, the situation is reversed with a large positive nitrogen and potassium balance, and unless adequate potassium salts are supplied, low serum potassium values are to be anticipated.

Low serum potassium values at some stage of the disease were found in over half of the cases studied. The detailed relationships between serum potassium, urinary excretions, and the nitrogen balance will be presented in a separate report in process of preparation.

The significance of potassium deficiency in various conditions has recently received considerable attention, particularly in reports by Fenn,[5] Darrow[3, 4] and others.

The principal trends of alteration of electrolytes in the different phases are summarized diagrammatically in Charts 1 and 2, with explanatory comments in Table 5.

Summaries of laboratory findings in typical cases are shown in Tables 6 and 7 illustrative of the changes indicated in Charts 1 and 2.

From the experience gained in these studies, the

CHART 1 – MAJOR ELECTROLYTIC ALTERATIONS IN ACUTE HUMAN POLIOMYELITIS

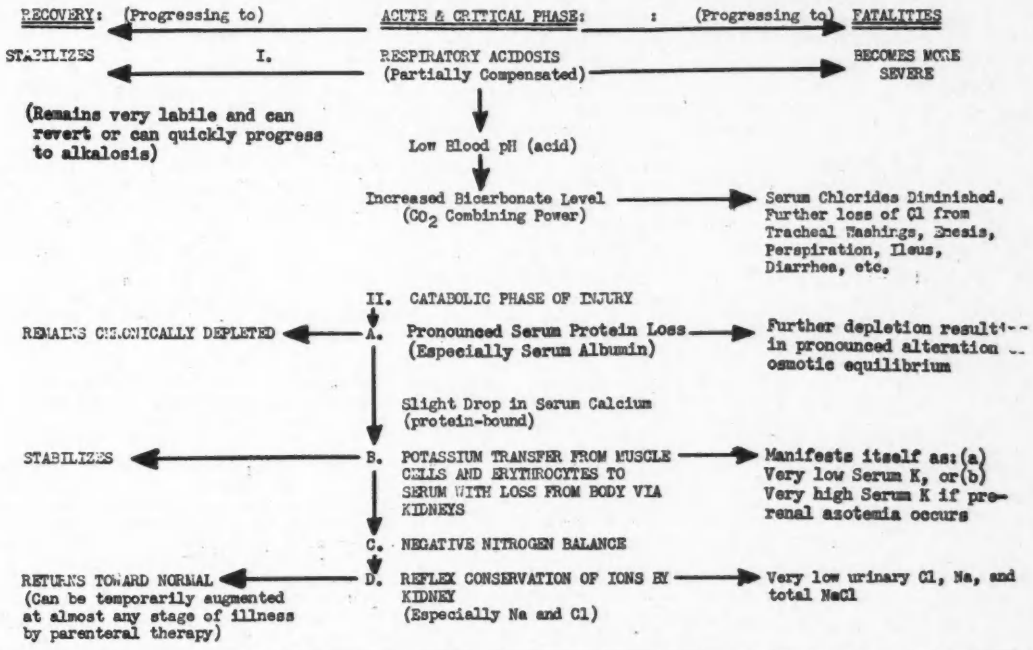
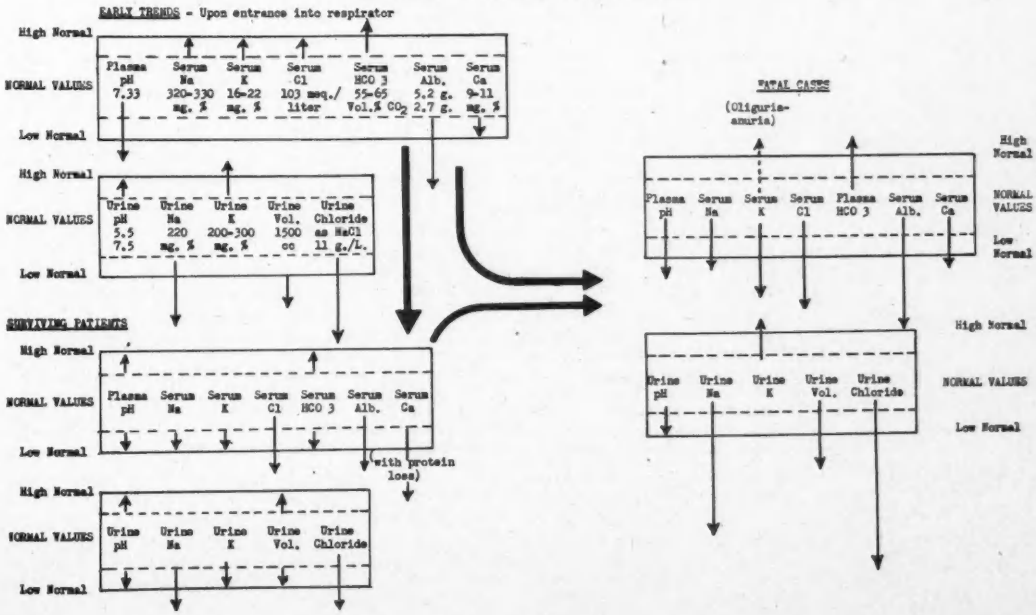

RECOVERY: (Progressing to)
ACUTE & CRITICAL PHASE: (Progressing to) FATALITIES
STABILIZES
I.
RESPIRATORY ACIDOSIS (Partially Compensated)
BECOMES MORE SEVERE
(Remains very labile and can revert or can quickly progress to alkalosis)
Low Blood pH (acid)
Increased Bicarbonate Level (CO_2 Combining Power)
Serum Chlorides Diminished. Further loss of Cl from Tracheal Washings, Emesis, Perspiration, Ileus, Diarrhea, etc.
II. CATABOLIC PHASE OF INJURY
REMAINS CHRONICALLY DEPLETED
A. Pronounced Serum Protein Loss (Especially Serum Albumin)
Further depletion results in pronounced alteration osmotic equilibrium
Slight Drop in Serum Calcium (protein-bound)
STABILIZES
B. POTASSIUM TRANSFER FROM MUSCLE CELLS AND ERYTHROCYTES TO SERUM WITH LOSS FROM BODY VIA KIDNEYS
Manifests itself as: (a) Very low Serum K, or (b) Very high Serum K if prerenal azotemia occurs
C. NEGATIVE NITROGEN BALANCE
RETURNS TOWARD NORMAL (Can be temporarily augmented at almost any stage of illness by parenteral therapy)
D. REFLEX CONSERVATION OF IONS BY KIDNEY (Especially Na and Cl)
Very low urinary Cl, Na, and total NaCl

CHART 2 – ELECTROLYTE TRENDS IN ACUTE HUMAN POLIOMYELITIS
(Patients confined to Respirators)



following recommendations are made with respect to the usefulness of laboratory determinations.

1. For patients requiring a respirator, frequent determinations of plasma pH and bicarbonate should be performed. The necessity of anaerobic handling of the specimen and the effect of temperature on the measurement of pH should be noted in avoiding errors in pH measurements.

2. Plasma protein determinations, particularly of the albumin fraction, should be done at 24- to 48-

TABLE 5.—*Electrolyte and Other Changes in Acute Poliomyelitis: Probable Mechanisms, Explanations, Correlations*

SUBSTANCE OR REACTION	PROBABLE MECHANISMS, EXPLANATIONS, AND CORRELATIONS
1. Plasma pH	Initially, the majority of patients when placed into the respirator have partially compensated respiratory acidosis. This is correlated with the elevated blood bicarbonate. It is due to insufficient or incomplete pulmonary aeration which may be caused by atelectasis, pulmonary edema, obstruction to airways, or other causes. If the acidosis cannot be corrected, the patient soon dies. If the acidosis can be overcome, the blood pH appears to stabilize but the patient remains in a state wherein further acidosis or alkalosis ensues very easily in proportion to the mechanical factors governing respiration. Obstruction of the airway, atelectasis, pneumonia, etc., very readily throw the patient back into acidosis.
2. Plasma bicarbonate	Correlated directly to the blood pH and to the attempt of the body to maintain a normal pH.
3. Plasma chlorides	Initial values vary from a slight increase with dehydration to low-normal values when the patient is better hydrated. If the patient continues in respiratory acidosis, and the plasma bicarbonate increases, the chlorides drop rapidily to low levels. Much chloride is lost in the tracheal washings, in perspiration, in emesis, in diarrhea, and with ileus. Urinary chlorides are quite low.
4. Serum sodium	The initial values are within the upper limits of normal but fall to the range of low-normal with hydration. Subnormal values, when found, are not very low but range from 300 mg. per 100 cc. upward. Urinary excretion of sodium is very low consistently. Sodium conservation appears to be notable.
5. Serum potassium	The initial serum potassium values are in the high-normal range. With hydration, they may fall to definitely subnormal values. If the patient becomes oliguric or anuric, the serum potassium levels are very high, because of the prerenal azotemia and the inability of the kidney to excrete potassium. The excess potassium unquestionably is a manifestation of tissue destruction and movement of intracellular potassium to extracellular fluid. Early administration of parenteral fluids, especially glucose solutions, contributes heavily to the potassium shift. Because of inanition, dehydration, circulatory collapse, etc., it is a common practice to force parenteral fluids in large quantities. Clinically, when the potassium levels drop, the condition of the patient is the same as that of patients in diabetic coma: There is delirium, circulatory collapse, cyanosis, abdominal distention. When potassium salts are given by mouth, the delay before the appearance of potassium in the urine indicates the considerable deficit that had to be overcome. Urinary potassium is increased both relatively (to the sodium) and absolutely.
6. Serum albumin	There is a precipitous drop in total proteins, and especially in the serum albumin. This drop begins by the third day of illness and usually reaches its lowest level by the tenth day of illness. There has been no spontaneous tendency toward recovery noted in the severe cases. Actually, the globulins tend to rise, resulting in reversal of the albumin-globulin ratio. The phenomenon of the serum protein loss is dramatic, profound, and consistent. It is not associated with loss of albumin in the urine. It is the systemic manifestation of the catabolic phase of injury and may be a factor in the production of edema within the central nervous system.
7. Serum calcium	The initial values are within the range of low-normal. In the severe cases in which the patient lives, there is a slight drop from normal which is probably associated with loss of serum proteins and represents that portion of the calcium bound to protein.
8. Urinary pH	Variable, but generally in acid range.
9. Urinary sodium	Values are consistently very low. This remarkable sodium conservation continues until the patient is convalescent, but it can be altered toward normal with the parenteral administration of large volumes of saline solution. Whether the sodium conservation is associated with or correlated with the chloride loss, and consequent kidney conservation, is not known.
10. Urinary potassium	Consistently elevated. Although the blood serum potassium may give no clue, the urinary potassium level is high both absolutely and relatively to the urinary sodium. The withholding threshold of the kidney for potassium is very low. As no potassium was supplied exogenously in these studies, the excreted potassium must be derived from the erythrocytes and from muscle cells. It then finds its way into the serum and is excreted promptly via the kidney. The status of potassium deficit of the body can be evaluated by oral administration of potassium and successive serial urinary potassium determinations. Eventually, with correction of the deficit, excess potassium will be demonstrated in the urine.
11. Urinary volume	Proportional to the body hydration. Occasionally, oliguria or anuria will occur with a rise in the non-protein nitrogen level and with a rise in serum potassium. In that event the patient can live for only a short period unless urinary flow is reestablished quickly.
12. Urinary chloride	Generally decreased. The probable mechanisms are discussed under Item 9 in this table. Sodium is retained in the body. The chloride ion is also conserved by the kidney, especially since it is being lost through other portals—sweat, tracheal washings, emesis, diarrhea, ileus, etc.

hour intervals during the first ten days, and at less frequent intervals thereafter unless additional critical periods of illness occur which will cause further depletion of serum albumin.

3. A reasonably complete estimate of the relationships of the blood electrolytes may be obtained from the simultaneous determination of sodium, potassium, bicarbonate, chloride, protein, and pH values. The significance of abnormal findings will depend on the phase of the illness.

4. For replacement therapy, the daily determination of urinary sodium, potassium, and chloride output is of great assistance. Adequate urinary volume is very important.

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TABLE 6.—*Chemical Determinations in Fatal Cases*

Date	Blood/Serum Chemistry: Chloride mEq. per Liter	Plasma Bicarbonate Vol. % CO_2	Na mg. per 100 cc.	K mg. per 100 cc.	Serum Protein Grams/ 100 cc.	pH at 38°C.	Urine Chemistry: pH	Na mg. per 100 cc.	K mg. per 100 cc.	Chloride as (NaCl) gm. per Liter	Urinary Vol. 24 hr.
Patient: White male, age 14 years. Entered hospital Sept. 9, 1948; entered respirator Sept. 10, 1948.											
9-14	102	52	320	10	4.98	....	(Partially compensated respiratory acidosis)				
9-16	86	79	295	20	....	7.05	Died Sept. 17, 1948				
Patient: White female, aged 30 years. Entered hospital Sept. 12, 1948; entered respirator Sept. 15, 1948.											
9-15	110	51	325	13	6.37	7.29	....	107	180	....	....
9-20	96	69	330	19	5.93	7.19	....	....	....	....	....
9-21	95	58	....	....	5.34	7.15	5.8	....	....	....	Oliguria, cyanosis
9-21	98	94	330	28	5.13	7.26	Died Sept. 22, 1948				
Patient: White male, age 38 years. Entered hospital Sept. 2, 1948; entered respirator Sept. 4, 1948.											
9- 9	93	73	345	18	4.82	7.07	....	....	....	1.3	1660 cc.
9-10	....	....	....	....	....	....	....	....	....	.45	1175 cc.
							Died Sept. 11, 1948. Due to massive pulmonary emboli				
Patient: White male, age 33 years. Entered hospital Sept. 9, 1948; entered respirator Sept. 11, 1948.											
9-14	97	69	....	....	....	....	....	....	....	....	....
9-20	98	54	325	28	5.95	7.05	....	....	....	....	Anuria
9-21	88	31	....	....	5.61	7.05	N.P.N 300 mg. % (Metabolic acidosis). Died Sept. 21, 1948.				

TABLE 7.—*Summary of Laboratory Findings in a Typical Case*

Patient: White female, aged 32 years. Entered hospital Sept. 10, 1948; entered respirator Sept. 11, 1948.

Date	Blood/Serum Chemistry: Chloride mEq. per Liter	Plasma Bicarbonate Vol. % CO_2	Na mg. per 100 cc.	K mg. per 100 cc.	Serum Protein Grams/ 100 cc.	pH at 38°C.	Urine Chemistry: pH	Na mg. per 100 cc.	K mg. per 100 cc.	Chloride as (NaCl) gm. per Liter	Urinary Vol. 24 hr.
9-14	96	47	310	....	5.80	....	....	....	....	....	....
9-17	101	71	295	....	6.10	....	....	....	....	....	....
9-20	101	71	325	14	5.28	7.37	....	....	....	....	....
9-21	93	67	315	10	6.10	....	....	....	....	....	....
9-22	93	72	325	15	5.63	7.38	....	....	....	....	....
9-23	....	....	....	....	....	....	7.2	29	52	0.75	1070 cc.
9-24	84	83	330	16	5.18	7.30	5.8	81	248	0.73	?
9-27	100	55	300	15	A.-2.75 G.-3.45	7.40	7.3	....	....	....	1050 cc.
9-29	102	67	320	17	A.-2.93 G.-3.36	7.26	6.3	177	348	5.56	1050 cc.
10- 6	108	45	315	18	A.-3.11 G.-3.24	7.26	....	....	....	....	....
10- 8	100	88	310	18	A.-3.02 G.-2.32	7.32	....	....	....	....	....
10-11	99	85	310	16	A.-2.75 G.-2.92	7.41	....	....	....	....	....
10-13	97	78	315	20	A.-2.75 G.-3.07	7.29	6.7	53	161	2.02	1800 cc.
10-14	....	....	....	....	....	....	6.9	59	119	1.40	2650 cc.
10-18	106	70	....	....	....	7.38	....	....	....	....	....

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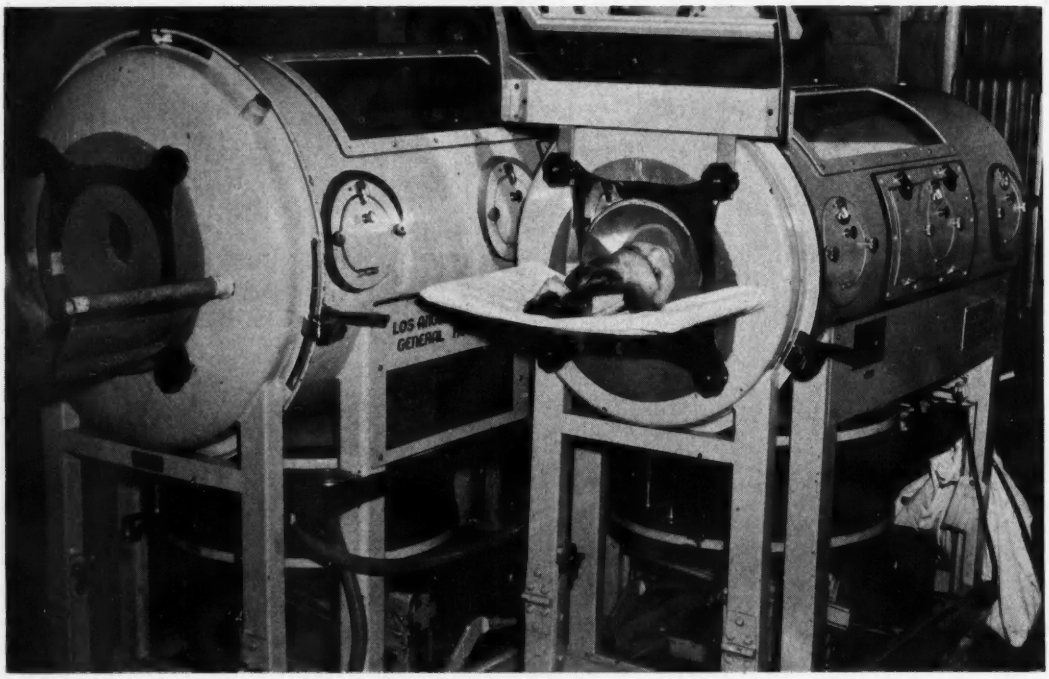
The New Junior Size Respirator



Despite the fact that three-fifths of all poliomyelitis cases occur in children under ten years of age, the various mechanical appurtenances devised to maintain respiration in patients requiring such assistance are designed for adults. The infant respirator is an exception, but very few infants contract the disease. Chest respirators come in all sizes, but at present they rarely furnish all factors required for the induction of maximum comfort and efficient respiration.

For these reasons, in 1948 the Drinker Collins Company was asked to manufacture a respirator for children between one and ten years of age. The machine produced is a replica of the adult model on a smaller scale. It has a larger motor and may be run at 50 cycles per minute. Otherwise it does not differ from larger ones, save in size. It has proven very satisfactory. Five of them were used throughout 1949 at the Los Angeles County General Hospital, and more are on order.

Likewise, a child's size rocking bed was made recently because the adult size is entirely unsuitable for children. It looks as though it might serve the purpose, but so far there has been no occasion to use it. The rocking bed has proven invaluable as an intermediate step in weaning adults from the respirator and returning them to the standard hospital bed when breathing has recovered sufficiently to permit it.

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Antihistaminic Drugs in Dermatology

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SUMMARY

From the results of treatment of 1,770 patients with dermatologic diseases (1,458 as reported in the literature and 312 observed by the author) it is concluded that antihistaminic preparations are of great value in allergic diseases where it is hypothecated that liberated histamine is the offender, as in acute edematous types of urticaria, erythema multiforme, and some cases of allergic pruritus.

The indiscriminate use of these drugs is to be avoided. Antihistaminic drugs are palliative—they do not cure. They often prolong the disease. They give temporary relief from swelling and pruritus. They develop no specific immunity and do not replace immunizing efforts. They do not replace or interfere with epinephrine or ephedrine.

THE present antihistaminic drugs are the outgrowth of the combination of many ideas and experiments. In 1910 Barger and Dale[2] isolated histamine from ergot and advanced the theory that the pharmacologic action of histamine on laboratory animals was similar to that noted clinically in anaphylactic shock. In 1932 Hill and Martin[10] presented a review of 165 experimental studies of nonspecific materials used to inhibit anaphylactic shock, none of which was considered sufficiently effective for therapeutic use. In 1927 the hypothesis that allergic reactions within tissue cells depend upon the liberation of a histamine-like substance was advanced by Lewis[13] in England. It was postulated that the union of antigen and antibody in sensitized cells results in the liberation of histamine normally present, which then produces an allergic response in all tissue by dilating the capillaries and causing a loss of plasma protein and fluid into the extracellular spaces. As this theory of the mechanism of allergic response gained acceptance, many investigators turned their efforts toward the development of a substance to neutralize, replace or displace histamine, thus short-circuiting the allergic reaction in the tissue cells.

The first preparation found to neutralize the effect of histamine both in living tissue and in the test tube was a phenolic ether, thymoxy-ethyldiethylamine (929 F), advanced by Fourneau and Bovet[6] in 1933.

In 1937 Bovet and Staub[22] advanced another formula, considerably more effective than thymoxy-ethyldiethylamine, known as n-phenyl-n-ethyl-n'-diethyl ethylene diamine 1571F. Unfortunately, both of these drugs were extremely toxic to human tissue and it was not until 1942 that Halpern[9] developed a substance which he called Antergan,® the chemical formula of which is dimethylaminoethyl benzyl analine. Antergan is unsuitable for general use in dermatology because it frequently produces undesirable reactions.

The first antihistaminic drug which was effective, yet non-toxic enough for general use was Benadryl® (betadimethylaminoethyl benzhydryl ether hydrochloride), reported by Loew[14] in February 1945.

The second histamine-neutralizing compound with relatively few side-reactions was Pyribenzamine® (n-pyridyl-n-benzyl-n-dimethylethylenediamine), reported by Mayer[16] in March 1945. This preparation appears to be about ten times as effective as Benadryl.®

The drugs in the approximate order of their effectiveness in relieving allergic symptoms are as follows:

1. Pyribenzamine®—n'pyridyl-n'-benzyl-n-dimethylethylenediamine monohydrochloride (Ciba Pharmaceutical Products, Inc.).
2. Benadryl®—beta-dimethylaminoethyl benzhydryl ether hydrochloride (Parke, Davis Company).
3. Trimeton®—1-Phenyl-1-(2 pyridyl) 3-dimethylaminopropane (Schering).
4. Hydryllin®—B-dimethylaminoethyl benzohydryl ether (Searle).
5. Thephorin®—2-methyl-9-phenyl-2, 3, 4, 9-tetrahydro-1-pyridindene hydrogen tartrate (Hoffmann-La Roche, Inc.).
6. Antistine®—2 phenylbenzylaminomethyl-imidazoline hydrochloride (Ciba Pharmaceutical Products, Inc.).
7. Neoantergan®—N-*P*-Methoxybenzyl-n'n-dimethylaminoethyl 2786 RP (Merck).
8. Antergan®—N'-dimethylamine ethyl N'-benzylaniline 2339 RP (Merck).

CRITERIA OF EFFECTIVENESS

Certain criteria now generally used to determine the effectiveness of an antihistaminic drug in laboratory animals give some measure of its effectiveness in man:

1. Its neutralizing effect of histamine on guinea pig intestine.
2. Ability to relieve histamine-induced asthma in guinea pigs.
3. Effect on anaphylactic shock.
4. Neutralizing effect of intravenous histamine and histamine artificially produced by horse serum in guinea pigs.
5. Prevention of wheals produced in rabbits by injection of histamine.
6. Toxicity quotient for animals such as dogs, rabbits, white mice and rats.
7. Effect on the blood and blood-forming mechanism.

However, the actual value of the drug in man must be determined by clinical use in a large group of patients with allergic disease, with attention to a few simple criteria:

1. Prompt alleviation of symptoms.

2. Recurrence of the symptoms upon withdrawal of the drug.

3. The substitution of a placebo for the drug should fail to elicit relief.

4. Patients should be under clinical control so that outside influences play no part in the response of the drug.

5. No other medication should be used in conjunction with the antihistaminic under investigation.

The position of antihistaminic drugs in dermatology cannot be determined without reporting all known data concerning their clinical effects. In this presentation the author's own experience (Table 1), as well as a review of the literature (Table 2) is presented. Table 2 shows the disease, the type of antihistaminic drug used, the number of cases reported, the investigator reporting, the results observed, and the percentage improvement obtained.

SIDE REACTIONS

Side reactions occur in 33 per cent of patients. No attempt will be made in this presentation to differentiate the specific reactions from each drug, as the responses vary widely; the same drug may

TABLE 1.—*Report of Cases by the Author*

Disease	Antihistaminic	No. of Cases	Results: Excellent	Fair	Negative
Acute urticaria	Benadryl®	17	10	5	2
Angioneurotic edema	Pyribenzamine®	34	25	7	2
	Trimeton®	19	14	3	2

Summary	Total Cases	Number Improved	Per Cent Improved
Benadryl	17	15	88
Pyribenzamine	34	32	94
Trimeton	19	17	89
	70	64	91

		No. of Cases	Excellent	Fair	Negative
Chronic urticaria	Benadryl	8	4	1	3
	Pyribenzamine	11	7	2	2
	Trimeton	7	5	....	2

Summary	Total Cases	Number Improved	Per Cent Improved
Benadryl	8	5	63
Pyribenzamine	11	9	82
Trimeton	7	5	71
	26	19	73

		No. of Cases	Excellent	Fair	Negative
Erythema multiforme	Benadryl	3	3	....	....
	Pyribenzamine	2	2	....	....

Summary	Total Cases	Number Improved	Per Cent Improved
Benadryl	3	3	100
Pyribenzamine	2	2	100
	5	5	100

		No. of Cases	Excellent	Fair	Negative
Atopic eczema (neurodermatitis)	Benadryl	82	27	31	24
	Pyribenzamine	22	9	8	5

Summary	Total Cases	Number Improved	Per Cent Improved
Benadryl	82	58	71
Pyribenzamine	22	17	77
	104	75	72

		No. of Cases	Excellent	Fair	Negative
Dermatitis venenata	Pyribenzamine	23	8	3	12

Summary	Total Cases	Number Improved	Per Cent Improved
Pyribenzamine	23	11	48

(Continued on next page)

TABLE 1 (continued)

Disease	Antihistaminic	No. of Cases	Excellent	Fair	Negative
Pruritus ani	Pyribenzamine	31	16	8	7
	SUMMARY		Total Cases	Number Improved	Per Cent Improved
	Pyribenzamine		31	24	77
		No. of Cases	Excellent	Fair	Negative
Infantile eczema	Benadryl	12	4	3	5
	Pyribenzamine	18	11	4	3
	SUMMARY		Total Cases	Number Improved	Per Cent Improved
	Benadryl		12	7	58
	Pyribenzamine		18	15	83
			30	22	77
		No. of Cases	Excellent	Fair	Negative
Post-scabetic pruritus	Pyribenzamine	13	7	2	4
	SUMMARY		Total Cases	Number Improved	Per Cent Improved
	Pyribenzamine		13	9	69
		No. of Cases	Excellent	Fair	Negative
Dermatitis Herpetiformis	Pyribenzamine	5	....	2	3
	SUMMARY		Total Cases	Number Improved	Per Cent Improved
	Pyribenzamine		5	2	40
		No. of Cases	Excellent	Fair	Negative
Erythema induratum	Pyribenzamine	3	....	1	2
	SUMMARY		Total Cases	Number Improved	Per Cent Improved
	Pyribenzamine		3	1	33
		No. of Cases	Excellent	Fair	Negative
Pemphigus	Pyribenzamine	2	....	....	2
	SUMMARY		Total Cases	Number Improved	Per Cent Improved
	Pyribenzamine		2	0	....

produce stimulation in one patient and sedation in another. Apparently reactions vary with dosage as well as with individuals. Persistent use and variation of dosage will often relieve undesirable reaction. Prolonged use of the drug is not advisable without frequent medical supervision.

The main reactions are: Insomnia; drowsiness (50 to 60 per cent); fatigue, lethargy; dizziness; faintness, weakness; headache (10 to 15 per cent); stimulation; nausea (2 per cent), gastrointestinal disturbances; urinary frequency with cystitis (1 per cent); emesis; dryness of throat, and dermatitis medicamentosa. In dermatitis medicamentosa, the eruption appears as a fine, papulovesicular rash which is clinically indistinguishable from the rash of measles.

It is seldom necessary to completely discontinue the use of an antihistaminic because of side reactions. In cases in which reactions cause extreme discomfort to the patients, another type of antihistaminic drug can be substituted and when necessary several changes may be made in order to find an antihistaminic drug which will relieve the patient without producing an objectionable side reaction.

In many cases the side reaction of drowsiness is of definite benefit. Benadryl appears to give more sedation than any other antihistaminic drug. When insomnia or itching is present it is often advisable to use Pyribenzamine during the day and Benadryl at night.

DISCUSSION

Because angioneurotic edema and acute urticaria are manifested by an acute and sudden edema, they seem particularly susceptible to the replacing or displacing phenomenon attributed to the antihistaminic drugs. In 739 reported cases and in 70 cases in the author's experience, approximately 85 per cent of patients with acute urticarias responded well. Of 278 cases of chronic urticaria reviewed and 26 in the author's series, improvement was shown in 77 per cent. The results of therapy are extremely difficult to evaluate in a disease in which the cause is so variable.

The therapeutic usefulness of an antihistaminic drug may be judged by its effect in patients with chronic urticaria which has persisted for several months despite the use of all other known therapy. If recurrence results immediately after withdrawal of the drug, the possibility of direct histamine desensitization should be considered. As the antihista-

minic drug does not produce immunization, chronic urticarias with specific antibodies are often prolonged, allowing the clinician to fall into a false sense of security. The lack of response may be explained by several factors: Inadequacy of the compound, improper dosage, or too early cessation of treatment. On the other hand, the high incidence of response may be partially explained by spontaneous recovery or by recovery because of coincidental topical applications, rest, sedation, calcium or epinephrine compounds.

Pruritus ani and vulvae are usually caused by allergic reactions to chronic infection. Infectious, pathologic and neurotic factors must be eliminated before the antihistaminic drugs will be effective. Eliminating those cases which are primarily from dermatitis venenata as a result of enemas, douches or medication, the most common causes of pruritus vulvae and pruritus ani are bacterial, monilial or fungous infections. The constant and prolonged infection of the anus with bacteria or fungus produces maceration and eczematization which will eventually lead to a sensitization of the skin to the organism itself, or to the products of secretion, or the products of destruction of the organism. This phenomenon has been called allergy symptom complex to infection, the infection apparently setting up an epidermal hypersensitivity which manifests itself in the form of pruritus.

If the antihistaminic agent controls itching, the itching complex fixation might not develop and the condition of the skin would be improved because

TABLE 2.—*Review of Literature Including Cases Observed by the Author*

Disease	Antihistaminic	No. of Cases	Reported by	Results: Excellent	Fair	Negative
Acute urticaria	Benadryl®	15	O'Leary & Farber[18]	9	5	1
Angioneurotic edema	Benadryl	18	Curtis & Owens[4]	11	....	7
	Benadryl	10	Lynch[15]	9	1	....
	Benadryl	35	O'Leary & Farber	20	12	3
	Benadryl	62	Spain & Pflum[21]	54	....	8
	Benadryl	9	Morrow[17]	7	....	2
	Benadryl	17	Foster	10	5	2
	Pyribenzamine®	34	Osborne, Jordan, Rausch[19]	23	10	1
	Pyribenzamine	84	Arbesman[1]	79	....	5
	Pyribenzamine	12	Kesten[12]	11	1	....
	Pyribenzamine	403	Spain & Pflum	323	....	80
	Pyribenzamine	8	Morrow	7	....	1
	Pyribenzamine	34	Foster	25	7	2
	Hydryllin®	24	Spain & Pflum	12	....	12
	Trimeton®	4	Spain & Pflum	4	....	....
	Trimeton	19	Foster	14	3	2
	Thephorin®	7	Frank[7]	6	....	1
	Thephorin	2	Frank	1	....	1
	Antistine®	12	Hughes[11]	8	....	4

Summary	Total Cases	Number Improved	Per Cent Improved
Benadryl	166	143	86
Pyribenzamine	575	486	85
Hydryllin	24	12	50
Trimeton	23	21	91
Thephorin	9	7	78
Antistine	12	8	67
	809	677	84

				Excellent	Fair	Negative
Chronic urticaria	Benadryl	35	O'Leary & Farber	25	7	3
	Benadryl	8	Shaffer[20]	7	....	1
	Benadryl	7	Curtis & Owens	3	....	4
	Benadryl	10	Lynch	8	2	....
	Benadryl	13	Lynch	11	....	2
	Benadryl	75	O'Leary & Farber	48	17	10
	Benadryl	8	Foster	4	1	3
	Pyribenzamine	15	Osborne, Jordan, Rausch	9	....	6
	Pyribenzamine	115	Arbesman	78	....	37
	Pyribenzamine	11	Foster	7	2	2
	Trimeton	7	Foster	5	....	2

Summary	Total Cases	Number Improved	Per Cent Improved
Benadryl	156	133	85
Pyribenzamine	141	96	68
Trimeton	7	5	71
	304	234	77

(Continued on next page)

the trauma of scratching would be removed. The author[5] reported the interrelated action of pruritus ani, seborrheic dermatitis and dermatophytosis in a previous paper.

In 74 cases of atopic eczema from the literature and 104 observed by the author, 60 per cent of the patients showed improvement after antihistamine therapy. In a few instances the eruption cleared and the patients were symptom free; however, in the majority the improvement consisted only of the control of itching. Because of the lack of uniformity of procedure among the various investigators, the only definite conclusion is that the various antihistaminic agents control pruritus when given in proper doses, thereby allowing other standard therapy an opportunity to clear the clinical manifestations of the disease.

In 119 reported cases of dermatitis venenata of all types, approximately 54 per cent of the patients obtained relief from itching but no change in the clinical appearance of the dermatitis.

There are available at present drugs which experimentally have antihistaminic and prophylactic usefulness as well as palliative action against skin manifestations of allergic disease. The relief of itching and the sedation help to control the patient and thereby increase the effectiveness of the normal therapeutic measures. The experimental work to date indicates that the antagonists of histamine in no way interfere with the antigen-antibody reaction and must not be confused with desensitization.

The antihistaminic drugs and histamine enter into a competitive relationship in that they compete for the site of action normally involving histamine, whether it be in a muscle cell, glandular cell or other type of cell. This may be called competitive inhibition. The antihistaminic agents undoubtedly act better when employed prophylactically than when employed therapeutically or correctively. The author has observed that in many instances the patient has been temporarily relieved by the drug but the interference with the immunity-creating mech-

TABLE 2 (continued)

Disease	Antihistaminic	No. of Cases	Reported by	Excellent	Fair	Negative
Erythema multiforme	Benadryl	4	Lynch	1	2	1
	Benadryl	3	Foster	3	....	....
	Pyribenzamine	2	Foster	2	....	....
	SUMMARY			Total Cases	Number Improved	Per Cent Improved
	Benadryl			7	6	86
	Pyribenzamine			2	2	100
				9	8	90
				Excellent	Fair	Negative
Atopic eczema (neurodermatitis)	Benadryl	12	Morrow	4	6	2
	Benadryl	82	Foster	27	31	24
	Pyribenzamine	16	Osborne, Jordan, Rausch	8	1	7
	Pyribenzamine	21	Arbesman	12	....	9
	Pyribenzamine	20	Morrow	4	14	2
	Pyribenzamine	22	Foster	9	8	5
	Thephorin	5	Frank	3	....	2
	SUMMARY			Total Cases	Number Improved	Per Cent Improved
	Benadryl			94	68	72
	Pyribenzamine			79	56	71
	Thephorin			5	3	60
				178	127	71
				Excellent	Fair	Negative
Dermatitis venenata	Benadryl	4	Morrow	2	....	2
	Pyribenzamine	15	Osborne, Jordan, Rausch	....	....	15
	Pyribenzamine	20	Arbesman	6	....	14
	Pyribenzamine	16	Kesten	10	....	6
	Pyribenzamine	33	Morrow	29	....	4
	Pyribenzamine	23	Foster	8	3	12
	Thephorin	4	Frank	2	....	2
	Antistine	4	Hughes	4	....	....
	SUMMARY			Total Cases	Number Improved	Per Cent Improved
	Benadryl			4	2	50
	Pyribenzamine			107	56	52
	Thephorin			4	2	50
	Antistine			4	4	100
				119	64	54

(Continued on next page)

TABLE 2 (continued)

Disease	Antihistaminic	No. of Cases	Reported by	Excellent	Fair	Negative
Dermographism	Pyribenzamine	4	Kesten	3	1	....
	SUMMARY			Total Cases	Number Improved	Per Cent Improved
	Pyribenzamine			4	4	100
				Excellent	Fair	Negative
Pruritus ani	Benadryl	9	Lynch	6	3	....
	Benadryl	8	Morrow	5	....	3
	Pyribenzamine	90	Frankfeldt[8]	57	....	33
	Pyribenzamine	4	Arbesman	3	....	1
	Pyribenzamine	15	Kesten	10	5	....
	Pyribenzamine	17	Morrow	3	10	4
	Pyribenzamine	31	Foster	16	8	7
	Antistine	5	Hughes	5	....	....
	SUMMARY			Total Cases	Number Improved	Per Cent Improved
	Benadryl			17	14	82
	Pyribenzamine			157	112	71
	Antistine			5	5	100
				179	131	73
				Excellent	Fair	Negative
Physical allergies (heat, cold, sunlight)	Pyribenzamine	6	Kesten	5	....	1
	Pyribenzamine	2	Osborne, Jordan, Rausch	2	....	....
	SUMMARY			Total Cases	Number Improved	Per Cent Improved
	Pyribenzamine			8	7	88
				Excellent	Fair	Negative
Infantile eczema	Benadryl	12	Foster	4	3	5
	Pyribenzamine	7	Arbesman	4	....	3
	Pyribenzamine	18	Foster	11	4	3
	SUMMARY			Total Cases	Number Improved	Per Cent Improved
	Benadryl			12	7	58
	Pyribenzamine			25	19	76
				37	26	70
				Excellent	Fair	Negative
Serum sickness reactions	Pyribenzamine	8	Kesten	6	2	....
	SUMMARY			Total Cases	Number Improved	Per Cent Improved
	Pyribenzamine			8	8	100
				Excellent	Fair	Negative
Insect bites	Benadryl	11	Lynch	4	4	3
	Pyribenzamine	1	Osborne, Jordan, Rausch	1	....	....
	Pyribenzamine	2	Arbesman	2	....	....
	SUMMARY			Total Cases	Number Improved	Per Cent Improved
	Benadryl			11	8	73
	Pyribenzamine			3	3	100
				14	11	79
				Excellent	Fair	Negative
Dermatitis medicamentosa	Pyribenzamine	10	Morrow	4	4	2
	Benadryl	2	Morrow	1	....	1
	SUMMARY			Total Cases	Number Improved	Per Cent Improved
	Pyribenzamine			10	8	80
	Benadryl			2	1	50
				12	9	75

(Continued on next page)

TABLE 2 (continued)

Disease	Antihistaminic	No. of Cases	Reported by	Excellent	Fair	Negative
Nummular eczema	Pyribenzamine	12	Morrow	3	7	2
	Benadryl	1	Morrow	....	1	....

SUMMARY	Total Cases	Number Improved	Per Cent Improved
Pyribenzamine	12	10	83
Benadryl	1	1	100
	13	11	85

Disease	Antihistaminic	No. of Cases	Reported by	Excellent	Fair	Negative
Post-scabetic pruritus	Pyribenzamine	12	Morrow	6	6	....
	Pyribenzamine	13	Foster	7	2	4
	Benadryl	7	Morrow	2	4	1

SUMMARY	Total Cases	Number Improved	Per Cent Improved
Pyribenzamine	25	21	84
Benadryl	7	6	85
	32	27	84

Disease	Antihistaminic	No. of Cases	Reported by	Excellent	Fair	Negative
Statis dermatitis with absorption phenomena	Pyribenzamine	12	Morrow	1	7	4
	Benadryl	5	Morrow	1	3	1

SUMMARY	Total Cases	Number Improved	Per Cent Improved
Benadryl	5	4	80
Pyribenzamine	12	8	67
	17	12	71

Disease	Antihistaminic	No. of Cases	Reported by	Excellent	Fair	Negative
Dermatitis herpetiformis	Pyribenzamine	4	Morrow	....	1	3
	Pyribenzamine	4	Osborne, Jordan, Rausch	3	....	1
	Pyribenzamine	5	Foster	....	2	3
	Benadryl	2	Morrow	....	1	1

SUMMARY	Total Cases	Number Improved	Per Cent Improved
Pyribenzamine	13	6	46
Benadryl	2	1	50
	15	7	47

Disease	Antihistaminic	No. of Cases	Reported by	Excellent	Fair	Negative
Seborrhea	Pyribenzamine	4	Morrow	4	....	....
	Benadryl	3	Morrow	....	2	1

SUMMARY	Total Cases	Number Improved	Per Cent Improved
Pyribenzamine	4	4	100
Benadryl	3	2	67
	7	6	86

Disease	Antihistaminic	No. of Cases	Reported by	Excellent	Fair	Negative
Erythema induratum	Pyribenzamine	3	Foster	....	1	2

SUMMARY	Total Cases	Number Improved	Per Cent Improved
Pyribenzamine	3	1	33

Disease	Antihistaminic	No. of Cases	Reported by	Excellent	Fair	Negative
Pemphigus	Pyribenzamine	2	Foster	....	....	2

SUMMARY	Total Cases	Number Improved	Per Cent Improved
Pyribenzamine	2	0	....

anism of the body has to some extent prolonged the course of the disease. It is generally admitted that the present antihistaminic drugs are not altogether ideal, as they are not effective in allergic manifestations of all types, nor are they universally useful in any particular syndrome.

Caution and infinite patience must be exercised in the evaluation of the clinical response to any drug —caution because of the tendency of the clinician to interpret results according to a predetermined purpose, and patience because no two people respond in like manner either physiologically or mentally. The subjective response varies with environmental, educational, racial and physical abnormalities of the patient. The role of histamine in the production of allergic responses varies with each patient as well as with the shock center involved.

The use of the antihistaminic drugs does not alleviate the necessity for thoroughness in investigation or the use of fundamental knowledge of the care of allergic dermatoses.

It would seem that the various antihistaminics give their best results when used to relieve allergic pruritus, and for this reason alone they fill a specific need in the dermatologic armamentarium.

The author's experience with the antihistaminics in the form of an ointment or cream has been so lacking in relief of symptoms that he has discontinued their use in that form.

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Asthma in Children—Problems in Diagnosis

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SUMMARY

Bronchial asthma in children may be difficult to diagnose. Education of the parents regarding allergic conditions, specifically bronchial asthma, is exceedingly important in order to assure satisfactory treatment and clinical results.

Chest symptoms of unexplained origin in early life should immediately arouse suspicion of allergic disease. Other causes of asthmatic symptoms must be borne in mind and excluded before a positive diagnosis of bronchial asthma is established.

Of the many factors to be considered in investigating a child with asthma, a comprehensive history is most essential. The climate to which the patient is exposed and the psychic influences must be taken into account. Physical examination, x-ray films and laboratory procedures should be carefully executed. Skin testing, especially with food allergens, should not be relied upon to give all the information in allergic disease. Some form of diet trial, such as elimination diets, should be used if sensitivity to food is suspected.

A HISTORY of allergic disease during childhood is found in 50 per cent of adults who have bronchial asthma. During childhood, bronchial asthma is the most frequent of the various manifestations of allergic sensitivity. Thus it is evident that the problems involved in diagnosing asthma in children are of primary importance.[13]

The onset of asthma in small children does not always follow the pattern typically seen in older individuals and for this reason it is undoubtedly overlooked in many cases. A definite diagnosis may be in doubt for a considerable length of time and through several attacks. It must be established by eliminating the various other conditions that may cause wheezing and dyspnea. Once the diagnosis has been made, many physicians tend to minimize the condition to the parents in the hope that the disease will not recur and that as the patient grows older he will cease to have asthma. It has been proved that the earlier an allergic state is recognized the easier it is to control and, if properly treated, the less liable it is to be a problem in later life.

The treatment of asthma in children is a somewhat different problem than that encountered in adults. In the first few years of life, the symptoms and physical findings are completely objective. It is the family rather than the patient who must be convinced of the need for therapy. Often there have been signs of other allergic manifestations, such as eczema or nasal allergic disease, which have conditioned and prepared the family for the diagnosis of bronchial asthma. The physician who makes the original diagnosis must satisfy the family that the illness is actually an allergic problem and that bronchial asthma is not just a cold, bronchitis or croup.

Several attacks, possibly of increasing severity, may have to occur before the family is convinced. After the diagnosis has been established the question of cause arises, and the all-important problem of educating the parents regarding allergic diseases begins. They should be told that asthma tends to recur and particularly that it is rarely cured but can be controlled. It is essential that they recognize that the disease will demand prolonged observation and therapy and that specific treatment of bronchial asthma in childhood is of definite value. If the treatment of all children with asthma were considered a perennial problem, the results of therapy would be greatly enhanced. In this respect, the experience of most allergists is in agreement with the conclusions drawn by Flensborg[4] in Denmark. According to Flensborg's study, children not receiving specific therapy were more prone to repeated attacks of bronchial asthma and other allergic manifestations than those who were specifically treated.

The tendency to wait to see if the child will outgrow the allergic state is born of wishful thinking and is not based on sound clinical observation. In one series,[2] asthma developed in 50 per cent of eczematous children. This observation spotlights the fallacy of the common saying, "Don't worry, Mother, the baby will outgrow his eczema."

Asthma becomes a significant problem in children before the age of five years. The average age of onset is between two and four years. It occurs more frequently in boys than in girls. The classical sequence is colic, starting most commonly about the age of three weeks; atopic dermatitis (infantile dermatitis) starting a few weeks later; recurrent upper respiratory infections, starting between the ages of two and three years, followed by the development of pollenosis or perennial allergic rhinitis and finally bronchial asthma.[6] Chest symptoms of unexplained origin in early life should immediately arouse suspicion of allergic disease.[7] During this period allergic edema rather than smooth muscle spasm is dominant; the spastic element does not develop char-

acteristically until the child grows older. At times noisy breathing and loud rales are the only signs of the condition. Bronchial asthma may not be indicated by physical findings present at the time of examination. The diagnosis must be made by means of history, skin testing and laboratory studies.

SYMPTOMS

The symptoms of bronchial asthma in children differ from those in adults as follows: (a) Asthma in children may only cause dyspnea or rapid breathing; (b) the asthmatic infant may appear comfortable, even when lying flat on his back. The absence of orthopnea can cast doubt on the diagnosis of asthma; (c) the absence of anxiety in the infant is particularly noticeable when compared to the feeling of apprehension common in the adult.

TYPES OF ASTHMA

Bronchial asthma in children is of two types, paroxysmal and chronic. The symptoms of both types are varied degrees of wheezing, dyspnea and coughing. The clinical course in the paroxysmal group largely depends on the efficiency and success of treatment. Chronic asthma, the condition which is most wearing for the patient and his family, is extremely difficult to control and treat satisfactorily.

The most common complications of long continued bronchial asthma in the child are emphysema and a typical chest deformity.[1] Because of its resemblance to that caused by rickets, this deformity is termed asthmatic pseudorickets. Bronchiectasis[17] also may prove a complicating factor.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of bronchial asthma is important. The many other causes of wheezing, dyspnea and coughing which must be kept in mind are as follows:

1. *Asthmatic bronchitis* in children is characterized by coryza, fever and poor response to ephedrine and epinephrine. There is a predominance of eosinophils in nasal smears and an accelerated blood sedimentation rate. It may be followed by bronchial asthma. Fever may be present with bronchial asthma alone, but may also arise from secondary infection or from allergic reaction, especially to foods.

2. *Foreign bodies in the bronchus* sometimes may cause wheezing, coughing, or shortness of breath. X-ray, fluoroscopic and bronchoscopic examinations are mandatory when an obstruction is suspected.

3. *Pulmonary conditions arising from cystic fibrosis of the pancreas* do not respond to ephedrine or epinephrine. Poor absorption of vitamin A as indicated by vitamin A tolerance tests, diminution or absence of the pancreatic enzymes on duodenal drainage, and the finding of a high fat content in the stools make the differential diagnosis.

4. *Thymic asthma* is rare. Enlargement of the thymus gland is immediately evident in x-ray films of the chest, and the condition responds rapidly to roentgen therapy.

5. *Dust bronchitis,* which has been noted in the dust-bowl area of the Middle West, is due to inhalation of finely pulverized dust. The resultant coughing is explosive and intractable. Fever and wheezing may be associated with soft, patchy mottling of the lungs in x-ray films.

6. *Sighing dyspnea* due to hyperventilation is a functional disorder which may occur in older children. Physical examination shows no abnormalities. The chief complaint is the difficulty of getting a deep breath. The condition is not helped with epinephrine.

7. The possibility of mistaking *pertussis* for bronchial asthma must be remembered. Pertussis is characterized by a lack of response to ephedrine or epinephrine, an absence of eosinophils in the blood, by leukocytosis with relative lymphocytosis, and by growth of *H. pertussis* on culture.

8. *Bronchotetany* is rare but may cause dyspnea and wheezing. Intravenous injections of calcium relieve the symptoms.

9. *Cardiac asthma* rarely occurs in infancy or childhood. (White's[18] youngest patient was 18 years of age.)

10. *Lymphadenopathy and mediastinal tumors, including Hodgkin's disease,* may result in compression and constriction of some part of the respiratory tract, causing wheezing and coughing.

11. *Allergic bronchopneumonia or Loeffler's syndrome* may cause transitory infiltrations of the lungs which can be revealed by x-ray examinations of the chest. A very high blood eosinophilia usually accompanies this condition. Miller and Piness[12] reported a series of cases of such allergic bronchopneumonia.

12. Frequently, mild (sometimes even severe) bronchial asthma in childhood is confused with pseudo-bronchopneumonia, infectious bronchitis or croup. On the other hand, actual pneumonia must be recognized and may be superimposed upon allergic bronchitis or bronchial asthma.

INVESTIGATION

There are many factors that must be considered in making a diagnosis of bronchial asthma in a child. A physician has the responsibility of reviewing the condition of the patient not only from a laboratory standpoint but as a whole. To accomplish this, the following factors should be taken into account:

History: It is hardly necessary to stress the great importance of obtaining a detailed history — one which includes data on psychological and environmental influences and the various other allergic manifestations as well as the family background. A detailed dietary history is of the utmost significance. This record should reveal dislikes or disagreements for specific foods and any possible imbalance of diet. A careful study of environmental and occupational surroundings also is essential when inhalants are suspected. Several conferences with the

parents may be necessary, as many details are not remembered on the first visit.

Effect of climate: Temperature, humidity, altitude and seasons have varying effects on bronchial asthma, especially when rapid climate changes occur. Schutzbank[16] recently found that 72 per cent of a series of patients with allergic disorders were benefited by living in Tucson, Arizona. The beneficial effects of inland, dry areas on allergic disease caused by foods, as well as decrease or abatement of the condition in the summer, as reported by Rowe,[14] has been confirmed in the author's experience. The explanation of these geographic influences is obscure. The benefit of summer weather probably depends on the sun's radiation.

Psychosomatic factors: The psychic aspects of asthma in children are difficult to evaluate. A majority of the behavior problems of the asthmatic child can be explained on a physical basis,[5] although this is not invariably true. Therefore, treatment of the psychic problem may be as significant as the program of hyposensitization or any other therapy. For example, some children, in order to gain attention, will dominate the home or schoolroom by actually precipitating or simulating acute cough, wheezing or asthmatic attack. Whether these children have an actual attack of asthma is difficult to establish. Control of the psychic influences may make the difference between good and poor control of an asthmatic child. For this reason, the exact influence of psychic problems must be evaluated for each patient and an endeavor made to rectify any contributory condition. Every attempt should be made to allow the child to lead as normal a life as possible and to make him feel that he is secure. This should be particularly reflected in the parents' attitude. Henderson[8] wisely suggested that "healthy neglect may even be preferable to over-solicitude."

Physical examination: Physical examination must be such as to uncover not only bronchial asthma but other manifestations of allergic reaction. The child should be carefully scrutinized for evidence of focal infections and other diseases. An x-ray examination of the chest, and, in older children, of the sinuses, should be routine. It must be remembered, however, that between attacks of asthma, there may be no abnormality observed in examination of the lungs.

Laboratory procedures such as examination of nasal smears and differential count of blood cells may be of some help in establishing the diagnosis.

Skin testing: The knowledge gained from skin testing is secondary in importance to that obtained from a detailed history. In the author's opinion, however, information can be gained from skin testing that could not possibly be elicited in any other way. Opinions differ regarding the number of tests which should be done. In recent "Letters of the International Correspondence Society of Allergy,"[11] the question was asked, "How many and what type of skin tests do you consider essential in a case of bronchial asthma?" The opinions ranged from doing nearly no tests at all to the extreme of making several hundred tests. The method of skin testing also varied.

There is also a question as to the value of skin tests in very young children. Skin reactions are much less likely to be evident in the first two years of life. Some physicians believe that skin testing is of no value in the first year of life. The author believes it often gives some clue to skin test infants in the first two years of life for reaction to the foods they have in their limited diets and for reaction to inhalants they may encounter. The method used is to screen the patient with scratch tests for response to the allergens felt to be important for the child. If the patient does not respond to the scratch tests, intradermal tests are rarely used for patients less than six years of age, and then for only the very important inhalant allergens. The information gleaned from tests with foods is by no means as reliable as that with inhalants. Moreover, there are children who are definitely sensitive to inhalants, and especially to foods, who do not have reaction to skin tests. The number of allergens with which a child is tested should increase as his age increases. Passive transfer tests may at times be indicated. Ophthalmic and nasal membrane tests have little value in determining the cause of allergic disease in children. The size of the reaction to skin testing has no bearing on the importance that the allergen causing the reaction may play in the child's condition.

FOODS

The problem of allergic sensitivity to foods in children is of paramount importance. The fact that foods can cause asthma in children cannot be disputed.[10] There is considerable difference of opinion as to the frequency of this sensitivity and its relative importance to recurrent respiratory infections, sensitization to pollens and other environmental allergens. Certainly, during the first few years of life, food sensitivities play a major role as a cause of allergic bronchial disease. A history of colic, vomiting and diarrhea, or of many changes in the food formula in early life, suggests the possibility of food sensitivity. Because of the limited number of foods in the diet in infancy, the study of possible allergenic foods is not difficult. Soya milk and the strained meat formulae offer complete substitutes for cow's milk. Potato and tapioca can be used in place of cereal. Many vegetables and fruits can be utilized. Thus, with processed foods, food substitutes and synthetic vitamins, nutrition and weight can be amply protected. Our experience confirms the reported frequency of allergic reaction to milk, eggs and the cereals, along with other less commonly offending foods such as fish, chocolate, citrus fruits, bananas and apples.

Here again, there is a difference of opinion. Hill[9] feels that asthma is rarely caused by allergic sensitivity to food. Cook[3] expressed the opinion that no more than 20 per cent of the cases of asthma in children are due to food. The author's experience leads to the belief that sensitivity to food plays the

chief role in bronchial asthma during the first five or six years of life.

Hill[10] recently discussed the danger inherent in test-negative diets. A five-year-old girl was brought to him with a typewritten list of "good" foods typed in black, and "bad" foods typed in red. The classification had been determined by skin tests. Tests had been done with 236 foods, including squab, tripe, calf brain, venison, caviar, poppyseed, elderberry, pheasant, chives and Limburger cheese. The child had had reaction to 109 of them, including Sanka coffee, rutabaga, German celery, thyme, cranberry, sand-dabs, tripe, sweetbreads and watercress. Among the foods she was allowed to eat were pheasant, guinea-hen, venison, horsemeat, turtle, abalone, caraway seed, juniper, avocado, mango and quince. This shows how far afield test-negative diets can go.

To determine the exact influence of any one food upon an asthmatic state is not easy, because of the many complicating and contributing factors involved. There is a great variance of tolerance to food at various times of life. The mother of a child with allergic disease may know some of the foods that produce asthma and often may have omitted them from the child's diet before skin tests were done.

Diet trial has a definite place in evaluating allergic response to foods. Because of the inadequacy of skin testing, some kind of diet trial must be used. Elimination diets such as those outlined by Rowe[15] are of definite help, particularly if they are modified as indicated by the history and skin testing of the patient. Such diets eliminate the most common offending foods and establish a definite program with detailed menus and recipes. If the mother is instructed carefully and the diet is followed in detail, nutrition and weight are well protected.

INHALANTS

In infancy and early childhood inhalants play a less important role than do food allergens. Inhalants become more important as age increases. Most of the children who react to pollen also react to house dust.

BACTERIAL ALLERGY

True bronchial asthma due to sensitivity to bacteria is rare in children. However, infections of any type may activate or increase allergic manifestations. Therefore, eradication and control of infections is required for the benefit on the allergic state and also for the child's general health.

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Anticoagulant Therapy in Heart Disease

A Summary of the Literature

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SUMMARY

Considerable experience by many independent workers with the use of anticoagulants in the treatment of certain types of heart disease has shown that such therapy reduces significantly the incidence of thromboembolic complications and, largely through this effect, the morbidity and mortality rate from heart disease of these types.

This is certainly established in acute coronary occlusion with myocardial infarction and in those instances of rheumatic heart disease with auricular fibrillation in which repeated embolic phenomena have occurred. The case for the administration of the anticoagulants in congestive heart failure is less secure, although there is no doubt that the number of thromboembolic complications is reduced by use of them.

The administration of the anticoagulants requires considerably more exacting attention than does the administration of the majority of therapeutic agents in use commonly today. Hence, it is suggested that the use of anticoagulants in heart disease be restricted to those instances in which the indications are clear and facilities are compatible with the efficient and safe use of the drug, whether Dicumarol or heparin.

THE use of the anticoagulants in the prevention and treatment of thromboembolic phenomena clinically is well established.[1,10,11,13,15,18,38] Hines and Barker[10] assert that "anticoagulant therapy is the best method for preventing thrombosis and embolism which is available at present." They list the following situations in which the use of anticoagulants may be advisable in chronic cardiovascular diseases:

A. Treatment of single episodes of thrombosis, or embolism.

1. Acute arterial occlusion (including coronary artery occlusion).
2. Acute thrombophlebitis, or phlebothrombosis.
3. Pulmonary embolism, or infarction.

B. Prevention of recurring episodes of thrombosis.

C. Long-term treatment of the disease (only in certain situations).

This summary is confined arbitrarily to the use of the anticoagulants in heart disease and omits reference to use of them in diseases involving primarily the vascular system outside the heart.

ANTICOAGULANT THERAPY IN ACUTE CORONARY OCCLUSION WITH MYOCARDIAL INFARCTION

The use of anticoagulants in the prevention and treatment of coronary thrombosis with myocardial infarction was suggested by Best and co-workers in a report on a series of animal experiments on intravascular clotting. These investigators produced intravascular clots in systemic veins by both mechanical and chemical methods. They demonstrated that the incidence of such artificially produced intravascular clots could be reduced dramatically by the use of heparin.

In 1938, Solandt and Best[29] produced coronary thrombosis regularly in experimental animals by injecting a solution of sodium ricinoleate into an isolated coronary artery. A thrombus formed in almost every instance when no heparin was used. When the animals were heparinized prior to the injection of ricinoleate, thrombus formation was a rare occurrence.

Solandt, Nassim and Best[30] produced large mural thrombi in the left ventricles of experimental animals by ligating the anterior descending branch of the left coronary artery and injecting sodium ricinoleate into the subendocardial myocardium. A large mural thrombus formed promptly and consistently when the animals were not heparinized. When heparin was given well before the experiment, no mural thrombi formed.

Heparin or Dicumarol* was used clinically in individual cases, or in small series of cases of coronary occlusion with myocardial infarction during 1941 and 1942. The first American report concerned exclusively with the use of Dicumarol in acute coronary occlusion appeared in December 1945 when Wright[34] described experience with 76 patients. Between the time of that report and 1949, approximately two dozen series of cases were reported in the American literature. As reflected in the literature, the greatest experience with this means of therapy was obtained by Peters and Brambel[26, 27] in Baltimore, by Nichol[19, 20,23] in Miami, by Parker and Barker[24, 25] at the Mayo Clinic, and by Wright and his associates[35, 36, 37, 39, 40] in New York City.

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*Dicumarol is the registered collective trademark of the Wisconsin Alumni Research Foundation which controls the use thereof.

The results obtained, while consistently favorable, were in no instance based upon a sufficient number of cases, nor upon sufficiently well controlled case material to warrant statistical analysis. They did, however, justify the more extensive study carried out by the American Heart Association's committee for the evaluation of the anticoagulants in the treatment of coronary occlusion with myocardial infarction.

THE AMERICAN HEART ASSOCIATION STUDY

Members of this committee, associated with the 16 hospitals in which the patients included in the study were treated, observed over 1,000 cases of coronary occlusion with myocardial infarction. Somewhat fewer than half of the patients were treated by conventional methods alone. The others received anticoagulants as well. A record of each case was forwarded on master forms to the central office at the New York Hospital where it was studied and the data tabulated for intensive statistical analysis.

A definitive report on the 1,031 case reports accepted for analysis is being prepared and will be published as a monograph. The data and conclusions quoted here are those contained in the preliminary report of the committee based upon a gross analysis of the first 800 cases collected.[39, 40] Comparable figures based upon the total 1,031 cases are known to be not significantly different and to support the same conclusions.

Twenty-four per cent of the control group and 15 per cent of the anticoagulant-treated patients died during the six-week period of observation. Deaths following one or more thromboembolic complications occurred in roughly 10 per cent of the control group and in 3 per cent of the treated patients. Deaths not preceded by a clinically recognized complication occurred in approximately 14 per cent of the control group and in 12 per cent of the treated group. Anticoagulants reduced the death rate largely by reducing the number of deaths due directly or indirectly to thromboembolism.

The death rates by week of illness were highest during the first two weeks, but were still considerable through the fourth week. For each period the death rate for the control patients was significantly higher than that for the treated group. To give maximum protection, anticoagulants should be continued for at least four weeks after the last thromboembolic episode.

The greatest reduction of mortality was in patients 60 years of age or older. While the crude death rates for patients under 59 years of age in both the treated and control groups did not show a significant difference, the incidence of thromboembolic complications was high in the younger age groups and the incidence of thromboembolic complications was much lower in the treated than in the control group.

Twenty-five per cent of the control patients and 11 per cent of the treated patients had at least one thromboembolic complication. However, in the treated group, the first complication developed in 3.5 per cent of patients before they had received any anticoagulant and 1.5 per cent during the first three days of anticoagulant therapy, before Dicumarol is ordinarily fully effective. Thromboembolic complications developed in only 6 per cent of the patients during the time they were under the full effect of anticoagulant therapy.

The number of thromboembolic complications diagnosed clinically per 100 cases was 36 in the control group and 14 in the treated group. Only 6.5 thromboembolic complications per 100 treated cases occurred in patients who were under the full therapeutic effect of anticoagulant therapy. This figure includes some complications in patients who were not under adequate anticoagulant therapy at the time the complication occurred.

The highest incidence of thromboembolic complications among the control patients occurred in the age group between 50 and 59 years, in distinct contrast to the death rate by age groups. Apparently, younger patients have thromboembolic complications commonly but are able to survive them. Older patients are more liable to succumb to the first thromboembolic attack. This indicates the importance of preventing thromboembolic phenomena in all age groups. Within the treated group, when distinction is made between those patients who were and those who were not receiving anticoagulants at the time of the complication, the effects of anticoagulant therapy are further emphasized.

When the rates of thromboembolic complications by week of illness are considered, the advantage of using anticoagulants is clearly demonstrated through the first four weeks of the illness. Since it is impossible to predict during the first week whether thromboembolic complications will develop during subsequent weeks, it is important to give anticoagulant therapy to all patients with coronary occlusion and myocardial infarction unless specific contraindications exist.

Patients receiving Dicumarol had a distinctly better chance of escaping thromboembolic complications of every type and at every site than did those who received conventional therapy alone.

The incidence of severe hemorrhage resulting from anticoagulant therapy was extremely low. Of the 30 hemorrhages observed clinically, 15 were mild, 14 were moderate, and only one was severe.

EXPERIMENTAL OBSERVATIONS

Blumgart and his co-workers[4, 5] produced experimental myocardial infarction in dogs by ligating the anterior descending coronary artery. Dicumarol was administered to some animals, and heparin and Dicumarol to others, immediately following the operation, in order to determine if adverse myocardial changes might result from anticoagulant therapy. The animals were sacrified at various intervals and the heart was examined grossly and microscopically. Fourteen animals received Dicumarol only, three

received heparin for several hours postoperatively until the effect of Dicumarol was apparent, and 15 did not receive anticoagulants but served as controls.

The incidence and magnitude of hemorrhagic extravasations on the endocardium and pericardium and of miliary hemorrhages in the myocardium were similar in the treated and control animals. In the few dogs with excessively prolonged prothrombin time there was no increase in myocardial hemorrhages. The size of the infarcts and the rate and character of healing did not differ between the treated and control groups. No mural thrombi were found in either group of dogs. The development of collateral anastomoses between the coronary arteries was the same in both groups.

The investigators concluded that Dicumarol produces no adverse effect on the myocardium of dogs which might retard the healing or the development of collateral circulation in experimentally produced myocardial infarction.

Beattie and co-workers[3] determined the effect of Dicumarol upon experimental occlusion of the descending branch of the left coronary artery in dogs. Comparison of the control and treated groups showed similar electrocardiographic and pathological findings. Grossly and microscopically, there was no evidence of propagation of coronary thrombi or of formation of mural thrombi in either group. In appearance and size, myocardial infarcts were the same in one group as in the other. Hemorrhage into the infarcted areas was not prominent in either group. Electrocardiographic changes included, singly or in combination, RS-T segment displacements, changes in the direction of the T waves, ectopic rhythms and conduction disturbances typical of those in similar ligation experiments previously reported. Similar changes occurred in the treated and in the untreated animals.

LeRoy and Nalefski[14] investigated the influence of Dicumarol on the healing of experimental myocardial infarction produced by ligation of the descending branch of the left coronary artery in 32 dogs. Dicumarol was administered to 15 dogs, ten dogs served as controls, and seven died within 24 hours. The animals were sacrificed in from five to 21 days postoperatively.

Grossly there was no significant difference in the appearance of the infarcts at any stage of healing. Mural thrombi were not found in any heart. Microscopically, there was no obvious difference between the healing infarcts in the treated dogs and those in the controls. Serial electrocardiographic studies revealed no variation in the rate or character of the evolutionary changes. It was concluded that Dicumarol therapy does not have any demonstrable deleterious influence on the healing of experimental myocardial infarction in dogs.

LONG-TERM THERAPY WITH DICUMAROL

The administration of Dicumarol over long periods of time may be advisable as a prophylaxis against thromboembolism in patients who are predisposed to the repeated occurrence of thromboembolic phenomena. Anticoagulant therapy may be indicated for the remainder of the patient's life. The patient for whom this type of therapy is most definitely indicated is one with rheumatic heart disease complicated by valvular damage and auricular fibrillation with periodic release of showers of emboli to the pulmonary or peripheral circulation. Any patient with heart disease associated with auricular fibrillation or with an intracardiac source of emboli may be a candidate for prolonged anticoagulant therapy.

Wright[36, 37] reported briefly on a series of patients with rheumatic heart disease and auricular fibrillation who had experienced multiple emboli and to whom Dicumarol was given to prevent the further development of mural thrombi and the subsequent detachment of emboli.

Foley and Wright[8] reported in considerable detail on these and additional cases. A total of 19 patients had been on Dicumarol for periods of from five to 20 months (average 11 months). The favorable results were no less than dramatic and, in certain instances, patients who had been invalids and in constant fear of death prior to anticoagulant therapy, led completely normal, active lives thereafter.

Sprague and Jacobsen[31] reported a case in which a patient who had rheumatic heart disease with periodic arterial embolism remained free of thromboembolic complications during 11 months while under ambulatory treatment with Dicumarol.

It may also be advisable to administer anticoagulants over an indefinite period of time to patients with recurrent coronary thrombosis and myocardial infarction. In 1945, Wright[35] suggested that the question of continued use of Dicumarol as a prophylactic measure in patients who had experienced a coronary thrombosis warranted further study.

Foley and Wright[8] reported upon five patients who had coronary thrombosis with myocardial infarction and who were treated with Dicumarol for periods up to nine months. No thromboembolic or hemorrhagic phenomena occurred in these patients during the period of observation, and the patients led essentially normal, productive lives.

Nichol[20] and Nichol and Fassett[21] administered Dicumarol to patients with coronary artery disease over long periods of time. The report by Nichol and Fassett concerned five patients who had had multiple attacks of coronary thrombosis prior to the administration of Dicumarol for periods of from six to 32 months. One patient who was given Dicumarol for 21 months died of acute coronary occlusion which the authors attributed to lack of necessary control of anticoagulant therapy. A second patient had not had an attack for three years while Dicumarol was given, although he had had three attacks of acute coronary occlusion during the 13 months prior to the administration of the anticoagulant. The other three patients had been on Dicumarol for from six to seven months without recurrence of occlusion.

Nichol and Fassett noted a decrease in the amount of angina during the time these patients were taking Dicumarol. They expressed belief that long-term therapy with Dicumarol is rational and safe, providing the prothrombin time is determined carefully and at frequent intervals. Nichol stated that he had administered Dicumarol to 64 patients in 70 attacks of acute coronary thrombosis; 11 died, a mortality rate of 15.7 per cent. In 40 initial attacks so treated, there had been but one death.

Nichol and Borg[22] reported further experience with long-term therapy in 68 patients who had had one or more attacks of coronary thrombosis and/or myocardial infarction. At the time of report, 36 patients had been on Dicumarol for three to 12 months, 20 for one to two years, 11 for two to three years, and one for five years. Prothrombin time was determined at weekly intervals after the patient had become ambulatory and an attempt was made to maintain the prothrombin time at a value twice normal, the equivalent of a reduction in the prothrombin activity to between 10 and 30 per cent of normal. The dose of Dicumarol averaged 60 to 75 mg. a day. Hemorrhage occurred in one-fourth of the patients, usually due to the presence of some pathological lesion, or to an overdose of Dicumarol. In only three cases was anticoagulant therapy abandoned because of hemorrhage.

Nine patients discontinued therapy; two of them died later of recurrent attacks of coronary occlusion. Ten patients died while taking Dicumarol, and in six of those cases autopsy was done. There was a fresh coronary thrombosis, or an infarction, in two instances and a cerebral hemorrhage in one instance; in three cases death was ascribed to ventricular fibrillation or to congestive heart failure. In two of the four cases in which autopsy was not done, the patients died of recurrent coronary thrombosis. Of the 49 patients remaining on Dicumarol, all were active in business or household duties. Although four had had episodes of acute coronary insufficiency, infarction had not occurred, and uncomplicated recovery had followed. The patient who had been on Dicumarol for five years without an attack of coronary thrombosis during this time had had three attacks prior to anticoagulant therapy.

THE USE OF DICUMAROL IN CONGESTIVE HEART FAILURE

Patients with congestive heart failure are prone to develop thromboembolic complications which increase the morbidity and mortality of the disease. Kinsey and White[12] reported the presence of pulmonary infarction in 24 of 50 cases of congestive heart failure in which autopsy was done. Carlotti and associates,[6] in a study of pulmonary embolism in 273 patients admitted to the medical service of a hospital, found that the admission diagnosis in 104 instances was congestive heart failure.

Patients with liver damage are liable to have reduced plasma prothrombin activity and to react in an extremely sensitive manner to a given dose of Dicumarol (that is, they are liable to be "hyperreactors"). Reisner, Norman, Field and Brown[28] determined the prothrombin time in 100 male subjects before and following a single dose of 100 mg. of Dicumarol. No patient was selected whose prothrombin activity was not normal initially. The prothrombin time was determined on whole plasma each day until it had returned to normal. Extensive liver function tests were carried out and observations were made of the size of the liver, the presence or absence of ascites, and the presence and degree of congestive heart failure.

Depression of prothrombin activity to less than 60 per cent of normal occurred in 28 patients, 93 per cent of whom had evidence of liver disease or congestive heart failure. The patients with the most profound depression had extensive liver damage as indicated by the presence of ascites, hepatomegaly, positive reaction to cephalin flocculation tests and inverted albumin-globulin ratios. Among 33 patients with congestive heart failure, 14 (42.4 per cent) were "hyperreactors" as manifested by a depression of prothrombin activity to below 60 per cent following the single test dose of Dicumarol. Three of these patients had other liver disease as well. Twenty other patients with congestive heart failure (57.6 per cent), three of whom had other liver disease as well, did not have a reduction of prothrombin activity to less than 60 per cent of normal following the test dose of Dicumarol.

The high incidence of congestive failure among the hyperreactors to Dicumarol is evidence that hepatomegaly due to congestive failure indicates a physiologically deranged liver. This conclusion is supported by the results of liver function tests. It is also evident that the presence of congestive failure may alter the response to Dicumarol. The response to a single test dose of Dicumarol is a sensitive test of liver function.

Anderson and Hull[2] administered Dicumarol to alternate patients with congestive heart failure in addition to employing the usual conservative methods of therapy. Patients with plasma prothrombin activity of 50 per cent of normal or less at the time of admission ("low prothrombin group") were not given Dicumarol. The series consisted of 142 patients, consecutive and unselected except for a small number eliminated because of the presence of jaundice, severe angina, or azotemia. Sixty-one were given Dicumarol, 58 served as controls and 23 were in the "low prothrombin group."

There was no correlation between the degree of hepatic enlargement and the reduction of plasma prothrombin activity. However, in 43 per cent of the patients with an initially low prothrombin activity, congestive failure had been first observed more than a year previously, suggesting that the disturbance of prothrombin formation might be related to long-standing or recurrent hepatic congestion.

A reduction of prothrombin activity to 10 to 30 per cent of normal was attained in 52 (85 per cent) of the 61 patients given Dicumarol. Adequate reduction was usually attained within 48 to 72 hours, but

there was pronounced variation in response to Dicumarol in individual cases. Menadione® was given on six occasions when the prothrombin activity fell to below 10 per cent of normal and in each instance the prothrombin level returned promptly toward normal. Hematuria was noted microscopically in several instances, and gross hematuria once in the presence of an indwelling catheter. No serious toxic effects attributable to Dicumarol were observed.

The average duration of hospitalization was almost exactly the same in the three groups. The mortality rate in the treated group was 11 per cent, in the control group 18 per cent, and in the "low prothrombin" group 9 per cent.

Thromboembolism may have been a factor in the death of two patients in the treated group and of seven patients in the control group. One of the two deaths in the "low prothrombin" group may have been related to pulmonary embolism. Definite pulmonary embolism or acute pulmonary infarction occurred in five patients—three in the treated group (but before the first dose of Dicumarol was given) and two in the control group. All five patients recovered. If the proved, probable, and possible instances of thromboembolism, fatal and non-fatal, are pooled, the number of thromboembolic complications in the entire series of 142 cases is 14 (10 per cent). Five (8 per cent) occurred in the treated group and nine (15 per cent) in the control group.

Anderson and Hull summarized: Among 61 patients with congestive heart failure to whom Dicumarol was given, it was possible to reduce and maintain the prothrombin activity at 30 per cent of normal or less in 52 patients (85 per cent) without apparent harm. Among the 61 cases only two suggestive and no certain thromboembolic complications occurred following the administration of Dicumarol. In four patients who had had pulmonary infarction prior to the use of Dicumarol, no further episodes occurred after Dicumarol was given. The mortality rate was lower and the apparent incidence of thromboembolism less in the group of patients who received Dicumarol than was the case in a closely similar group of the same size in which no anticoagulant was employed; but there is no certainty that the difference in mortality rate is significant, or that the apparent difference in the incidence of thromboembolic complications is real.

All patients admitted to the Veterans Administration Hospital in Minneapolis because of cardiac decompensation were treated with Dicumarol after October 1946. The report by Wishart and Chapman[33] is a preliminary evaluation of the therapy as carried out in August 1947. Sixty-one patients with congestive failure were treated with Dicumarol. In 19 patients (31 per cent) auricular fibrillation was present and there were definite signs of mitral stenosis in 11 (18 per cent).

The prothrombin time was determined each day and the prothrombin concentration was kept between 10 and 30 per cent of normal. The average initial prothrombin concentration, before Dicumarol was started, was 62 per cent of normal and in one case it was only 17 per cent—evidence of seriously impaired liver function secondary to congestive failure. Dicumarol was administered in most cases until the patient was ambulatory or until death supervened. The average daily dose of Dicumarol for an adequate effect was 78 mg., confirming the view that patients in cardiac failure require smaller doses of Dicumarol than do compensated persons. No hemorrhagic complications developed, although it was often necessary to suspend Dicumarol therapy because of excessive depression of the prothrombin activity. Vitamin K was occasionally administered to counteract an excessive Dicumarol effect.

The mortality rate was 32.8 per cent (20 deaths) and 12 autopsies were done. There were no deaths definitely attributable to pulmonary embolism, and in 19 instances death was not suggestive of this complication. Emboli were not found in any of the 12 autopsies. Because of the difficulty of establishing the diagnosis of pulmonary embolism and infarction in every instance, symptoms and signs thereof were carefully sought and thoroughly investigated. Definite pulmonary infarcts developed clinically in two patients on Dicumarol therapy, but during a time when the Dicumarol effect was inadequate. Pulmonary and systemic infarcts were present in six of the 12 cases in which autopsy was done, but in five instances these lesions had developed before or after Dicumarol therapy. In one case pulmonary infarct developed despite adequate doses of Dicumarol.

With the clinical and postmortem evidence combined, it is probable that embolic phenomena developed in four cases (6.5 per cent) despite adequate Dicumarol therapy. Previously published reports indicate that in a group of comparable patients not given anticoagulants, the expectancy would be for pulmonary emboli in more than 20 per cent.

COMMENT

It is apparent that, with the exception of the American Heart Association study, there is no series of patients with heart disease who have been treated with anticoagulants which is of sufficient magnitude, or sufficiently well controlled, to warrant statistical evaluation. However, it ought not be ignored that in every series reported in the literature the results of treatment with anticoagulants have been favorable, consisting usually of a considerable reduction in the incidence of thromboembolic complications and of a more modest, although frequently significant, reduction in the immediate mortality, either in comparison with a control series, or with the anticipated occurrence of such complications and deaths as judged by the literature or the personal experience of the authors.

Nichol[23] observed recently that the composite mortality rate in 656* cases of acute coronary occlusion with myocardial infarction treated with anti-

*The aggregate of cases covered in eight independent reports in the literature (excluding the American Heart Association report and reports of series included in that study).

coagulants was 13.1 per cent. In contrast, he found that the immediate mortality rate for an aggregate of 2,325 cases† in which anticoagulant therapy was not used, was 28.8 per cent.

The use of the anticoagulants in the treatment of certain types of heart disease is based upon the frequent occurrence of thromboembolic complications and upon the importance of these complications in increasing the morbidity and mortality rate. The advocates of anticoagulant therapy cite the studies of Eppinger and Kennedy,[7] Nay and Barnes,[17] Wartman and Hellerstein,[32] Hellerstein and Martin,[9] and Mintz and Katz[16] as evidence that thromboembolic phenomena do complicate certain types of heart disease commonly and that they do significantly increase the immediate morbidity and mortality rates. To those critics who deny the importance of thromboembolism in the types of heart disease mentioned in this review, the answer is, obviously, that they must be overlooking such complications.

The essential problem at present is to attain means whereby the anticoagulants may be administered both effectively and safely to patients with heart disease. As has been acknowledged repeatedly, heparin and Dicumarol can be administered effectively and safely only in experienced hands and where suitable laboratory facilities exist. That hemorrhages do (infrequently) occur as a result of anticoagulants, and that they are often serious and occasionally fatal, is undeniable; but reports of such untoward reactions demonstrate beyond reasonable doubt that the greatest single factor in the production of hemorrhage in the circumstances is human error—erroneous diagnoses, careless or misguided administration, and failure to observe the meticulous management which is essential to the safe and effective use of these drugs.

There is no promise of simpler, more error-proof and more economical laboratory tests for following the course of patients being given anticoagulants. There is no immediate promise of a clinically useful and economical substitute for heparin, although Paritol® or some similar substitute may, in time, prove to be valuable. There is evidence, however, that the coumarin Tromexan®—the ethyl ester of di-(4-hydroxycoumarinyl) acetic acid—may prove to have certain distinct advantages over Dicumarol in clinical practice.

As a practical matter, it must be suggested that the physician who cannot administer the anticoagulants in an expert manner, who cannot obtain exacting laboratory control, and who cannot maintain close observation of patients, should avoid the use of anticoagulants except when the indications are absolute. He should probably use no other anticoagulant than heparin in those instances in which he does administer this type of therapy. He should not attempt to manage patients on long-term therapy but should refer them for that kind of preventive care.

†Aggregate of 14 series reported in the literature since 1940.

In circumstances in which laboratory control is precise and the physician can provide meticulous observation of the patient, the anticoagulants may be administered effectively and with a minimum of hazard from hemorrhage if the following essentials are observed in all instances: (1) accurate diagnosis; (2) determination of the clotting time or of the prothrombin time, according to the drug being used, before any anticoagulant is administered and each day thereafter until the response of the patient is clearly determined, whereupon such studies can be made on alternate days, twice a week, or, occasionally, at weekly intervals; (3) exacting laboratory control according to the rigid standards described by all workers in this field of therapy; (4) administration of the anticoagulant to produce the optimum therapeutic effect; (5) frequent and careful observation of the patient; (6) continued administration of the drug until the hazard of thromboembolism is removed. Anything short of these criteria will lead unnecessarily to failure and to the eventual disrepute of therapy of this type.

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Non-Directive Psychotherapy

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SUMMARY

Psychotherapy is a word to describe an age-old process. It would be better not to speak of psychotherapy, but of psychotherapies. Specialists are not the only ones who act as psychotherapists, since every human being fills this role at one time or another. Besides this, no two persons follow an identical approach. Finally, all therapists change technique constantly. The kinds of psychotherapy must therefore approach infinity.

Some physicians appear to assume that only one type of psychotherapy may claim a scientific basis. Although Freud first put psychotherapy on a scientific path, there is no reason to say that Freud must be the last in this field.

Over the past few years a new trend has started in psychotherapy which deserves close study. This new trend challenges some old beliefs and gives a new tool to help patients of some types. It is called non-directive or client-centered psychotherapy. This therapy does not try to solve the patient's problems for him, but rather establishes the conditions under which a patient can work out his own salvation.

Each year non-directive psychotherapy grows in importance. Much can be learned from the method.

TODAY every physician talks about psychotherapy, psychiatry and psychosomatic medicine. Much of this interest has come within the past ten years. Because of this recent prominence, it may be forgotten that what is described by the words psychotherapy, psychiatry and psychosomatic medicine goes far back in human history.

Much depends on what is meant by these words. Psychotherapy in its broadest sense implies that someone changes some of his actions or some of his thinking after contact with someone else. Applied too broadly this would include under psychotherapy some curious reactions, like the effect of a college girl in her Bikini bathing suit on her boy friend, or the influence of Hitler on Chamberlain in Munich. In each case someone brings about an effect on someone else by other than physical force.

It is not to be expected that everyone will like the same kind of psychotherapy. Generally speaking, the kind known best is the kind preferred. Patriotism works in somewhat the same way. Normal persons love best that country with which they are most familiar.

To show a few types of therapy in common use, three varieties can be touched upon — therapy of command, therapy of exhortation, therapy of reassurance. A therapist who commands will call upon some law to back him up, such as a divine law, a state law, or a "law" of human nature. A therapist who exhorts tries the "Dutch uncle" approach, telling the subject he owes it to himself, his family or his community to change his ways. A therapist who reassures may soothingly hypnotize with his constant denial that any real problem exists, and so lull the subject into a temporary peace of mind. Not a few psychiatrists use one or more of the above techniques at some time during therapy. So do parents.

When physicians think of the best psychotherapy most of them turn to the work of Freud and his followers. What Freud did can never be overestimated. He threw off the mantle of shame and superstition that had cloaked mental and nervous disease, and founded modern psychotherapy. But Freud did not stop all further advance.

Freud and his followers, through their writings and lectures, have been influential in popularizing the idea of psychotherapy. Psychoanalysis found a place in popular fancy, so that Hollywood and most laymen doubt they get their full money's worth without it.

Though psychoanalysts follow Freud more closely than others, in their ranks are variations. Some psychoanalysts, like Horney,[3] discard a few of Freud's pet theories. Any science or person shows a sign of growth if able to stand criticism. By refusing to hold too sacred everything Freud wrote, psychoanalysts can best imitate him who never in his life bowed to any authority.

Behind their diversity, psychoanalysts often seem to agree that they should control, or guide, or direct patients. Psychoanalysts also give the author an impression, perhaps a mistaken one, that psychotherapy calls for someone very wise, who knows most of the answers about humans, and who can vigorously direct patients in the best method to solve problems.

Non-directive or client-centered psychotherapy challenges some of these assumptions. The word "non-directive" follows a modern trend which also helped name other sciences like non-Euclidean geometry, non-Newtonian physics, non-Aristotelian psycho-logics (semantics).

A good way to introduce discussion of non-directive psychotherapy might be to compare it with parts of Dante's epic, "The Divine Comedy," which begins,

> In the midway of this our mortal life
> I found me . . . astray
> Gone from the path direct.

A physician today might prefer to say that "Dante was mixed up and in need of psychotherapy." In the poem, Virgil comes by fate to Dante's aid, and leads him through a frightening Inferno and Purgatorio. As Dante goes through these places, he learns much, and emerges a wiser, more adaptable man, ready for Beatrice to take him through the Paradiso.

If Virgil can be called a psychotherapist for Dante, it is worth noting that Virgil does not command, or exhort, or do much to reassure Dante. Most of the time Virgil walks along with Dante, calls attention to bits of interesting sadism going on, and names certain persons and places when asked. Dante, the patient, talks three times as much as Virgil, the therapist.

Some quotes tell what therapy Dante received: "My teacher [my therapist, Virgil] . . . with so composed a lip he listen'd ever to the sound of the true words I uttered." (Virgil can hold his lips tightly shut while Dante talks.) "Consult thy knowledge," says Virgil. (Virgil does not try to give all the answers.) "Now seest thou, son—" (Virgil often is content to point out something, with no explaining.)

Although Virgil talks, his words do not appear his main duty. When Dante hesitates to enter the Inferno:

> "And when his hand he had stretch'd forth
> To mine, with pleasant looks, whence I was cheer'd
> Into that secret place he [Virgil] led me on."

All through the poem when Dante turns in terror and despair to Virgil for comfort, Virgil seems to say this: "Yes, Dante, you see what you see. You are learning and seeing things you may not like. But you see reality, and you are scared. I know." When, in his agony, Dante pleads with Virgil, he is saying, "Tell me, Virgil, do you see what I see?" Then Virgil replies in substance, "It scares you, doesn't it?"

TECHNIQUE OF NON-DIRECTIVE PSYCHOTHERAPY

Like most psychotherapy, non-directive psychotherapy leans heavily on talk, on words. In non-directive psychotherapy a patient converses, expresses himself freely in words, on whatever topic he pleases. "Non-directive" give the clue. This does not mean that the therapist does nothing but stay awake. He must listen with care, and accept whatever emotion or feeling the patient expresses. To this emotion a therapist responds as to an emotion, not insisting very much on factual accuracy or falsity of words.

Words normally have a partly factual, partly emotional content. Each part may vary from less than 1 per cent to more than 99 per cent. For instance, what if a patient says, "My boss is a damn fool"? The therapist learns little fact about the boss. Factually he learns that the patient works under a boss. Surely no therapist will stake his reputation on the "fact" that the boss in question has a low I.Q. and is doomed to hell fire. From the phrase, "my boss is a damn fool," one fact relevant to therapy is learned: At that instant the patient hates his boss. Little fact, much emotion. Non-directive psychotherapy evaluates the emotional content of words, and responds to it. How? By accepting the emotion, not arguing about the fact.

In practice how might a therapist respond to the phrase, "My boss is a damn fool"? Certainly not, "Yes, I know the so-and-so. You put it mildly." Neither does he try to palm off some esoteric formula like, "You project your feelings in reference to your employer's dominance." In non-directive psychotherapy a possible response might be, "You are very upset with your boss right now." For one who likes a formula, non-directive psychotherapy begins like this: Evaluate the words of the patient, and respond to those words by showing acceptance of their emotional content. In other words, the therapist shows that he grants the patient the right to be upset. (He ought also to warn himself to distrust formulas.)

This looks pathetically easy. Yet even a very understanding physician may not find it so easy. Physicians too often fall into the modern habit of not hearing much of what others say. In our culture, conversation, in the sense of an attempt to understand one another, has become a lost art. A patient may stay so wrapped up in his own emotions that in turn he finds it impossible to fully grasp what a therapist may say to him. To make things worse, physicians have become expert talkers in vague generalities. As Francis Bacon put it, our words "are as the stars, which give little light, because they are so high."

Somewhere along the way, as most of us muddle through our schooling, we develop a blind trust in the literal or factual content of words. But no word can mean the identical thing to two persons, nor keep its identical meaning for the same person at different times. Although we grasp this more or less, we get fussed that words slither around, or get up and walk away like Alice's wickets. We tend generally to "ascribe to words an entirely false value and certitude which they cannot have."[6]

Words express our relation to things, in part intellectually, in part emotionally. When a communist froths at the mouth and calls all of us "American capitalistic slaves," he chiefly tells us that he himself is quite unhappy. Or as in the present furor over "homosexuals" in the government departments at Washington, the more fervid denouncers may be trying to exorcise their own homosexual impulses. To find words with an almost total factual content we read cook books ("add two eggs and stir"), or laboratory guides ("watch the solution boil and see what happens"). At the opposite extreme, when a patient says "Life is not worth living" the physician knows he is listening to emotion, 99 per cent plus.

Ability to listen to words compares to music appreciation. With no "ear" for music, we hear mostly a jumbled noise at a symphony. Some amateurs learn to pick out various movements. Trained musi-

cians can hear each instrument as it blends into the whole. Toscanini, they say, can hear one tiny, single false note. If perfect, non-directive psychotherapy would offer a patient an equally skilled, trained ear to catch every emotional tone. Probably few, if any, therapists can do this, but all can aim to do it.

Non-directive psychotherapy does not direct a patient in what he says, or when or how he says it. Often, for the first and only time in his life, a patient can talk freely, with someone to actually hear him. Meanwhile, as a patient expresses his feelings, he meets a warm reception, but with no praise and no blame. A non-directive therapist should be thought of not as a judge of another's misdemeanors, but as a realist who takes people as he finds them, and accepts them as such.

Those who analyze non-directive psychotherapy use phonograph records to follow along and explain what goes on. Many times records have caught every single word spoken by patient and therapist from first to last contact. When a therapist listens to himself speaking to a patient the chastening process is said to demand a lot of humility. Then, if never before, a therapist hears how much he talks, how vapid he may sound, how much direct pressure he exerts on the patient.

When we think about it, most of us can only marvel at our skill in saying the wrong thing. Take this horrible example. Once I visited a child with mumps. I had been the family physician for some time. On leaving the child's bed, I said something like, "Won't your dad look funny when he gets the mumps?" If you think that very unfunny, so did the family. They shifted to another doctor who had no delusions of being a humorist. You may call that family touchy, as I did. Yet all in all, could not my remark have been omitted to everyone's gain?

In non-directive psychotherapy, if never before, a therapist learns that every word counts, every word he utters will help or hurt. Careless talk has no place in non-directive psychotherapy. We doctors do take ourselves too seriously often enough, but we do not take seriously enough what we say to patients. We may imitate to our sorrow Alice in Wonderland: "At least—at least I mean what I say—that's the same thing, you know." "Not the same thing a bit," said the Hatter. In a certain field the Mad Hatter was not mad.

So in non-directive psychotherapy the patient finds he can express his feelings on any subject, self, family, relations, neighbors, employer, therapist. He decides what to take up, when, how, what to say or omit. The patient becomes the active one, the doer, the star of the show. As he finds the therapist accepts him and his emotions, he keeps on going, probes ever deeper. If the therapist opposes him, rejects him, directs him, he may flounder in a vague generality of words. A patient "knows" or "senses" what hurts him most, what he wants to talk about, how, and when each topic can bear to come to the surface. Prying often does more to harm than to help.

Who can profit by non-directive psychotherapy? Time will give the answer. No one claims that non-directive psychotherapy cures every nervous and mental problem. Non-directive psychotherapy does not try to replace psychoanalysis where "deep" therapy may be called for. On the other hand, it yearly seems able to extend its usefulness and help more and more patients. Where it will stop cannot be foretold. Rash claims of super-success and rigid limits to its use both alike appear unwise.

Some experts give definite criteria to select suitable patients: (1) A certain maturity of the patient, plus some ability to change. Both requisites occur most often in the age span from 15 to 50 years. (2) Average or superior intelligence. (3) No hopeless physical handicap. (4) No total dependence on others. (5) No overwhelming environment. (6) Enough emotional stress.[11]

STEPS IN NON-DIRECTIVE PSYCHOTHERAPY

Anyone who has ever tried to write a textbook has learned that in describing any process he often winds up with crude artifacts. For instance, every well-trained anatomist knows that the layers of pelvic fascia are mostly dissection artifacts. Yet books find it helpful to describe the "layers." In a similar way, if the point is not pressed, non-directive psychotherapy may be divided into steps. An expert, like Rogers,[11] will describe 12 steps in non-directive psychotherapy. I seem to recognize six steps. The exact number makes no difference.

1. *The Patient Comes for Help.* For therapy a patient seeks someone whom he hopes will help. Obviously. But why? Patients look for help only after emotional pressure builds up to a certain point. To open up and probe into our feelings in the presence of another person will beget some pain. And few, except mental masochists, court pain unless inner tension gets unbearable. Some day that may change, and patients may seek help earlier. But today most patients will endure a lot of grief before they feel the urge to pour it out. Patients do not have much idea of where to look for help, and their inertia holds them in a rut until pain makes them seek help. Also it wounds our pride to admit that we need assistance.

A therapist usually furnishes a place to talk. Patient and therapist decide on a time convenient to both. From the first a patient may act like a skater on thin ice, and hang back on the edge near shore. His wariness shows clearly if he has sought help elsewhere and failed to find it.

If a patient finds a friendly reception (experiences good rapport) with no restraint on how he expresses his feelings, the phase of exploration may end early in the first interview. Many techniques are reported needed for rapport. Basic to them all, I believe, is this—a therapist who has solved a major part of his own conflicts, who will sit quietly, without fidgeting, and listen with obvious care and interest.

While at college we used to describe a fellow

student as "a guy who hopes to find that heaven is one large ear." No doubt he needed a kindly therapist. One who can listen attracts us when we are upset. A listener, not a talker. Even Thomas à Kempis, the monkish author of "The Imitation of Christ," said, "I would that many a time I had kept silence."

2. *The Patient Expresses His Negative Feelings.* Once he feels safe, a patient begins to vent his hates, fears, anxieties, bewilderments. He feels something is wrong. He may not know why. So he tries to tell what he "thinks" about (that is, feels about) things. At first he tends to complain about other persons, or his symptoms. In this he skirmishes on the surface.

Should he find no rebuke, no one to condemn, he shifts to deeper problems, present problems. (Recall the woman of Samaria.[9]) He slowly brings up things he has not admitted to himself, or has long banished from awareness. He may start with blaming others, or with curses for his own tough luck. Before long he dismisses these surface irritants and turns to grapple with his real personal problems.

To pass through this stage takes a variable amount of time, depending on the amount and intensity of stored-up, repressed negative feelings, and the skill of the therapist. In one sense, "deep" therapy means "long" therapy.

Should a patient clam up, quiet, friendly waiting will often start him on once more. Or an occasional acceptance of his plight may be shown by such phrases as "It is not easy to talk about things that mean a lot to us, is it?" Non-directive psychotherapy seems to indicate that we do not have to tell a patient how deep to go into his problems. If we let him alone, do not try to decide where he goes, he will go fast enough, straight enough, and deep enough to suit his individuality.

3. *The Patient Expresses His Positive Feelings.* If the second phase goes well, a strange thing happens. At last, much of the patient's griping stops, sometimes not to return. A patient who began by crabbing at others, at fate and at himself, after a while stops. He has given vent to his feelings, and he feels as relieved as others do after a hearty belch.

To his feelings now, things start to get tolerable, or even worth praise. This about-face, from negative to positive, comes with nearly predictable certainty, if the therapist does not bungle technique. Just to watch this change-over proves again that some words contain mostly hot air. A salesman who spent hours damning his boss now begins to grant his employer some ability for running the office. A teenager who sneered at his dad now admits that his dad won election to office in the Elks. A man who called his wife less than a "dream girl" will now say that she does a beautiful family wash.

In this phase the patient finds symptoms less crushing, his own and others' defects less appalling, the future less bleak. When he can see some of the "good" with the "bad" he starts to achieve insight. He begins to take hold of reality. His emotional tension starts to relax. He accepts himself, his opinions, others and their opinions (even of him) more calmly. Emotional fog begins to lift.

A non-directive psychotherapist tries to accept positive feelings in the same way that he did negative feelings, with no praise, no blame. A therapist acts like a mirror. He reflects the patient's feelings, so that the patient can see himself in new perspective. Any observant person can find in the behavior of children many defects of their parents. In somewhat the same way a patient gradually sees in the therapist many of his own emotions, as he could never recognize them in himself, and with slowly increasing clarity. Yet as the patient reveals himself, a therapist, with his warm acceptance of a patient as he is, differs from the cold rigidity of a mechanical mirror.

4. *The Patient Explores Various Choices.* Once he has expressed his negative and positive feelings, a patient finds he is more free. He can start to consider what to do to change himself and his environment. Strong repressed emotions may destroy or restrict a normal tendency to grow. Ease tension, and growth reasserts itself. A more adaptable personality comes to the front as emotional fogging burns away.

Every modern analysis of how we learn confirms one fact. In learning anything, we hit a plateau every so often. We advance a bit, then level off for a time. Advance more, level off. Advance, level off. Non-directive psychotherapy also shows these plateaus at each stage. When a patient starts to explore various choices, a therapist often may feel like prodding him. Yet insight of the patient, not of the therapist, counts. Non-directive psychotherapy offers evidence that to explore and to choose counts only when done by a patient. Students do not always make the most progress merely by studying under a teacher loaded down by half a dozen degrees.

In his own good time, when he is ready, not before, a patient will decide. He will select what he wants, decide what he can do. His judgment may be astonishingly good. The wisest of therapists often show wisdom best in not offering much by way of solutions. This is one time when light shines very nicely under a bushel.

5. *The Patient Begins Positive Actions.* Once he makes his choice, the patient begins to act. He may be timid, slow. He may dawdle, only to elect such simple things to do that the therapist wants to explode a firecracker under him. After weeks or months of talk the patient may make the world-shaking choice to go to bed one hour earlier at night.

Right there is the point. *He chooses.* He stops drifting. The therapist notes to himself with approval not *what* the patient chooses, but *that* he chooses. For choice and act, like muscle, grow with exercise. No one lies in a sick bed for years, hops out and climbs Mount Wilson the same day. Ther-

apists are liable to the same mistake as parents who want to hurry the immature into maturity. But the immature cannot be hurried. Emotional growth, like pregnancy, may take nine months or more.

With the first small acts chosen, then performed, the patient gains confidence. He begins to show more definite progress. He starts to integrate his acts. When new behavior flows from his own insight and choice, it shows more zest and spontaneity than what he does by command or direction. We get most fun in life when we act as free agents along self-chosen paths.

6. *The Patient Decides to Stop Therapy.* This too falls under the patient's, not a therapist's, choice. The decision to stop depends on many factors, but chiefly that the patient has made several small choices, then carried them out. He feels a bulge or two where once was only flabby muscle. He gets elan from solving some problems to suit himself. He wants to use this new-found confidence. The future he can face unafraid (or less afraid) as he strikes out for himself.

Every chronically ill patient has some chronic nervousness. Often we doctors hang onto patients year after year, getting nowhere. Part of the fault is the patient's, who wants to make us a semi-permanent crutch. But every doctor takes the most pride in that patient who can carry on without further help.

Not that any patient will have solved every life problem the day he leaves his therapist. What counts is his confidence that he can see and answer (or try to answer) his problems. Again, growth does not stop with his last interview. During therapy growth begins, but does not end. In theory, growth continues for life.

If a patient overestimates himself, he may decide to return for further therapy at a later date. Or a new, paralyzing crisis may send him back. To decide to start, to stop, or to resume treatment is up to the patient. The choice is always his.

These six steps vary from patient to patient, for patients differ just as do houses one from another. But millions of homes have four definite parts—places to prepare food, to sleep, to loll, to take care of excretions. So non-directive psychotherapy tends to have certain traits in most cases.

Looking at the other side of the coin, we know that our education often began by some teacher's drumming rules into us. Next we learned so many exceptions that we doubted the value of rules. So the six steps here set forth need not be looked upon as revealed dogma.

THREE QUESTIONS

Three questions arise.

First, if non-directive psychotherapy offers so much, why does it attract so little notice or encouragement from the medical profession? None of my own medical friends seems to have heard of non-directive psychotherapy. At the Los Angeles County Medical Library, two librarians said they had not heard the term, and neither recalled any requests for articles or books on the subject. So I wrote to physicians all over the United States, including a few nationally known psychiatrists. None of those who replied claimed first hand knowledge of non-directive psychotherapy. Up until now I have read nothing about non-directive psychotherapy in any medical journal. A reliable source states that probably no medical journal has published an article about non-directive psychotherapy.

Why so little medical interest in non-directive psychotherapy? Most of the work has come from those outside the medical profession. Carl R. Rogers, Ph.D., and his co-workers have published the most significant papers. Dr. Rogers' book, "Counseling and Psychotherapy,"[11] seems to give the clearest introduction to non-directive psychotherapy. Since non-directive psychotherapy grew in non-medical surroundings, since articles on it were published in non-medical journals, and since the subject created no noisy public controversy, physicians may not yet have heard about it.

Second, does not a therapy that does not guide or direct patients sound absurd? Possibly so, to our ears. But we should not condemn any work on our prejudices. Physicians have ingrained habits of bossing patients, much of which is carried over into the psychotherapy they practice.

Listen to Freud.[2a] "I did not find it easy, however, to direct the patient's attention." "I was obliged to point out to the patient." "I continued my questions."

Psychosomatic medicine takes some direction for granted. "Psychoanalytic insight and guidance in management, combined with reeducation and reassurance prove adequate to handle the emotional factor in the majority of psychosomatic disturbances."[15]

A standard text says,[7] "The physician should proceed to give specific suggestions as to methods of cure." And, "Steady reassurance and encouragement by the physician are important during the early part of this retraining."

My former professor of psychiatry writes,[5] "The doctor's talk to the patient must be positive as well as frank." "The physician must have complete disciplinary control at all times." "Many patients will gain security by developing some dependency upon the physician for a time."

We can multiply such quotations. Yet when we take phrases out of context we risk a distortion of a writer's intent. But most psychiatrists insist uniformly on a dominant role by the therapist. If any author's meaning has been perverted here, it is unintended.

Third, did not Freud stumble upon psychoanalysis merely by letting a patient talk freely? I have heard this many times and have read it once in a while. It may help to look into this claim. One example from Karl A. Menninger, M.D.: "Their [that is, Breuer's and Freud's] discovery came about through a famous but anonymous patient. It was a woman who came in to be relieved of typical ner-

vous symptoms. The lady sat down to tell the doctor her troubles. . . . She had a fluent tongue. . . . By the time she had told her story in full, she was well."[8]

After considerable checking I can find no such origin for psychoanalysis. This is the story: Freud did not meet Breuer until about 1884, having worked in physiology and brain anatomy at least from 1876 to 1882.[4] Not until 1893 did Dr. Joseph Breuer and Dr. Sigmund Freud co-author a few pages in a German medical journal (Neurol.-Centralblatt) on "The Psychic Mechanism of Hysterical Phenomena." Two years later, in 1895, the same two workers put out their famous book, "Studies in Hysteria."[2] In this book we find the same paper of 1893, five case histories, theories by Breuer, an outline of psychotherapy by Freud.

The five case histories were the first ever published by Breuer and Freud. Case 1 told about a patient of Breuer's. Cases 2, 3, 4 and 5 discussed Freud's patients.

Case 1, that of "Anna O.," goes back to 1881. The patient was treated by Breuer alone, long before he met Freud (probably in 1884). Breuer used talking during hypnosis to treat Anna O.[2] "It was a great surprise to me, when for the first time, and accidentally, a disturbance, which had existed for a long time, disappeared in the evening hypnosis through an unprovoked conversation." "The surprising fact that from the beginning to the end of the disease all stimuli originating from the second state as well as their results, had been removed through talking in the hypnotic state." By "second state" Breuer seems to mean what we call the subconscious.

The patient in Case 2, that of "Mrs. Emmy von N.," came to Freud in May 1889. Freud[2] says, "I decided to treat her by that method of investigation in a state of hypnosis which I had learned from Breuer's history of his first patient."

Case 3 was that of "Miss Lucie R." Freud[2] first observed the patient "towards the end of 1892." "She had lost all perception of smell . . . was depressed . . . weak, complained of a heavy head, loss of appetite, and an incapacity for work." "The young lady visited me from time to time during office hours . . . showed a quite distinct general analgesia . . . the nasal mucous membrane was totally analgesic." "On attempting to hypnotize Miss Lucie R. she did not lapse into the somnambulic state. I, therefore, was obliged to forego somnambulism, and the analysis was made while she was in a state which did not perhaps differ much from normal."

Freud did not just listen. He speaks of his interviews with Miss Lucie R. like this: "I asked her." "I told her I did not believe . . ." "She quite agreed with me." "On questioning her . . ."

There can be little doubt that Miss Lucie R. was Freud's famous first patient in psychoanalysis. On Lucie he tried hypnotism, and failed. She and Freud talked, and she improved. With Lucie R. in 1892 psychoanalysis seems to have been born. Yet the sample quotations leave no doubt in my mind that Freud took his usual vigorous part in therapy. We do not see Freud listening passively while Lucie R. talked out her troubles. Nothing I have read of Freud's own works shows me that Freud ever had the idea of non-directive psychotherapy as we know the technique today.

A shrewd appraisal of Freud's approach to therapy is the following. "Freud was quite openly educating his patients in his early praxis, and doing it veiledly in his later praxis."[1]

OTHER POINTS ON NON-DIRECTIVE PSYCHOTHERAPY

1. Non-directive psychotherapy stresses the present. Often a patient can integrate himself without delving into childhood and infancy in minute detail.[11]

2. Non-directive psychotherapy does not use that state of great dependence of patient on therapist, which psychoanalysts call transference.

3. Non-directive psychotherapy favors a weekly interview of about an hour. The total number of interviews tends to be not excessive in number.[11]

4. Non-directive psychotherapy gives evidence that in properly selected cases the failures arise chiefly from blunders by the therapist.[11] This offers a challenge to any therapist's skill.

5. Non-directive psychotherapy demands no superhuman wisdom or unusual personality from the therapist.[11]

6. Non-directive psychotherapy stresses practical results more than theory.[11]

7. Non-directive psychotherapy questions the assumption that few of us can solve our own problems. Most of our mistakes come from emotional turmoil. Average persons have enough intelligence to work out many answers to their problems *if* emotions stop confusing them. Also modern educational theory holds that average persons can gain skill to make intelligent choices. Non-directive psychotherapy develops this skill in learning. Somewhere, some line must be drawn limiting how much and what others shall tell us how to think, how to feel. Non-directive psychotherapy tries to draw this line at the start, making the patient independent of the therapist's direction. This challenges some common modern trends.[12, 13, 14]

CONCLUSION

Our age did not invent psychotherapy. Every culture has tried to provide some make-shift in psychotherapy, some attempts better than others. Our oldest books, like the Bible and Homer, talk of people who knew that discussing one's problems with others would help bring relief. Over 300 years ago Don Quixote said to Sancho, ". . . since you have been running on like this with no one to stop you, you don't feel an ache in your entire body. Talk on, my son; say anything that comes to your mind or to the tip of your tongue."

Non-directive psychotherapy offers a new approach to this human trait, and tries to study condi-

tions which help or hinder success.[10] We do not know the limits of non-directive psychotherapy at present. In selected cases it has given excellent results.

Non-directive psychotherapy may revolutionize much of modern psychiatry, for it shows how to help patients in early stages of psychic disturbance with a minimum of time and maximum of efficiency. It may point the way to rational preventive psychotherapy which we need most of all. Non-directive psychotherapy also can give us hints on how to deal more helpfully with our patients in the everyday practice of medicine.

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CASE REPORTS

- Mediastinitis with Aortic-Esophageal Fistula Following Swallowed Fishbone—Pathogenesis, Diagnosis, and Prophylaxis
- Term Pregnancy Following Removal of Right Ovary and Left Corpus Luteum Cyst
- Hepatitis and Nephrosis Due to Cough Syrup Containing Chloroform

Mediastinitis with Aortic-Esophageal Fistula Following Swallowed Fishbone—Pathogenesis, Diagnosis, and Prophylaxis

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ALTHOUGH perforation of the esophagus by a foreign body with subsequent complications is discussed in detail in the American literature, there are only a few reports of perforation of the aorta secondary to such a lesion. A review of the literature and several isolated case reports have appeared recently in the foreign literature. Features presented in them were similar to those in the following case report. In the authors' opinion these features characterize a recognizable clinical syndrome calling for heroic therapy.

CASE REPORT

A 58-year-old white American female entered the hospital April 13, 1948, three hours after swallowing a bone from a "buffalo fish." The patient complained of sharp and constant pain in the thyroid region and in the mid-sternum with radiation to the interscapular region. The past and family histories were non-contributory. No significant abnormalities were noted upon physical examination. Repeated fluoroscopic and x-ray studies of the chest and esophagus after barium and barium-soaked cotton swallows revealed no evidence of the presence of a foreign body or of perforation. The patient was discharged the next day with instruction to return if further difficulty developed. Seven days later she was readmitted with complaint that during the week she had had intermittent aching pain at the xiphoid process and substernally beneath the angle of Louis, radiating to the interscapular region and intensified by the swallowing of solid food or liquids. Six hours before readmission the patient had vomited one to two pints of bright red blood, then had fainted and upon regaining consciousness had perspired freely. The temperature was 101° F., the pulse rate 90 per minute, and respirations 16 per minute. The blood pressure was 160 mm. of mercury systolic and 80 mm. diastolic. In a physical examination no significant abnormalities were observed. Hemoglobin content of the blood was 13 gm. per 100 cc. Leukocytes numbered 6,300 with normal cell differential. The urine was normal. Bleeding time, clotting time, non-protein nitrogen level and liver function profile series were all within normal limits. Esophagoscopy was carried out. There was no foreign body or bleeding point in the entire esophagus, but blood clots were observed immediately beneath the cricopharyngeus and a biopsy specimen from a thickened area 3 cm. below the cricopharyngeus was reported to show leukoplakia. Therapy consisted of parenteral administration of vitamins K and C, a transfusion of 500 cc. of whole blood, and sedation. The following afternoon hematemesis (900 cc.) occurred, and the patient immediately went into profound shock. Transfusion of 1,800 cc. of whole blood was required to raise the blood pressure to 130 mm. of mercury systolic and 90 diastolic. At this time, roentgenologic study of the upper gastrointestinal tract, which was carried out to determine the point of bleeding as a guide to surgical treatment, showed no definite esophageal lesion, although there appeared "to be extrinsic pressure, perhaps from glands in the mid-esophageal area." No varices could be demonstrated fluoroscopically. The stomach was dilated and apparently contained clotted blood. A circular defect along the greater curvature of the fundus was noted. Pronounced pylorospasm prevented filling of the duodenum. In view of the equivocal nature of the findings, operation was postponed, but after another uneventful 24 hours, hematemesis of approximately 1,000 cc. occurred. Exploratory laparotomy with wide gastrotomy and duodenal exploration was carried out but the source of bleeding was not found. For three days postoperatively the patient improved, then bleeding began again and deep shock ensued despite multiple transfusions. The patient died 19 days after swallowing the fish bone and 12 days after the first hemorrhage.

AUTOPSY

Significant findings at autopsy were limited to the esophagus and aorta. At the level of the fourth thoracic vertebra there were two irregular defects in the posterior wall of the esophagus (Figure 1). Each measured 5 mm. in diameter and they were 5 mm. apart. The adjacent esophageal wall was not indurated. The stomach was considerably dilated and filled with fresh blood and blood clots.

The esophageal defects communicated with a mediastinal hematoma 5 cm. in diameter and the mediastinal tissue surrounding it was indurated. Communicating with the hematoma at the junction of the arch and descending thoracic aorta in the anteromedial aortic wall and just medial to the origin of the left subclavian artery was an 8 mm. opening with smooth, slightly raised, rolled borders (Figure 2). The right subclavian and common carotid arteries originated directly from the arch of the aorta.

Numerous slightly calcified, occasionally ulcerated atheromatous plaques were observed throughout the aortic intima. There was no evidence of an aortic aneurysm.

Examination of the microscopic sections from the borders of the esophageal perforation showed acute inflammatory changes characterized by edema and heavy cellular infiltration (Figure 3). This infiltration consisted predominantly of polymorphonuclear leukocytes, but lymphocytes and mononuclear cells were also present. These changes involved

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all layers of the esophageal wall and were present to a lesser degree throughout the wall for some distance from the perforation. The esophageal perforation communicated with acutely inflamed and, in some areas, necrotic loose connective tissue of the mediastinum. This process led to acute aortic periarteritis and, in some areas, to acute panarteritis with necrosis of the entire aortic wall (Figure 4). Early atheromatous changes were also present in the aortic wall.

DISCUSSION

Barrie and Townrow[2] collected from the literature reports of 80 cases of perforation of the esophagus and aorta by a swallowed foreign body, and added a report of their own. In many of the cases the clinical features were such as those described by Chiari[3] in 1914—initial substernal pain, symptom-free interval of several days, "signal" hemorrhage, and fatal hemorrhage. The time interval between the esophageal perforation and death varied from five minutes to six weeks, with an average of approximately eight days. The "signal" hemorrhage preceded the fatal one by from two hours to three days, with an average of one day. Frequently pain recurred prior to the signal hemorrhage.

As to the mechanism of perforation of the aorta, Barrie and Townrow stressed the relationship between the character of the traumatizing object (blunt or sharp) and the time interval required for perforation. They expressed the opinion that sepsis does not play an important role. Pin prick perforation of the esophagus, resulting in infection with subsequent necrosis of the aortic wall and rupture due to internal pressure, was suggested by Watson-Williams.[8] Thrombosis of the vasa vasorum preceding necrosis with perforation of the aorta (as observed in carcinoma of the esophagus by Postoloff and Cannon[7]) may well play a role. No doubt, fatal

Figure 1.—Esophagus. The defect on the right has been extended. Note the hematoma.

Figure 2.—Aorta. Microscopic section taken at point directly opposite arrow.

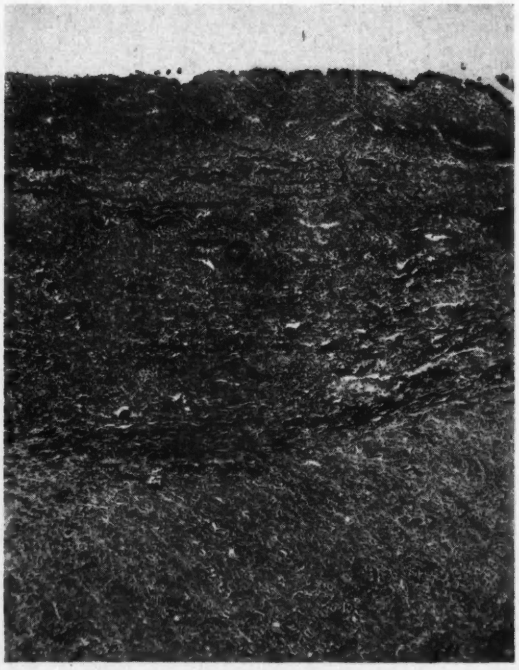

Figure 3.—Esophageal wall.

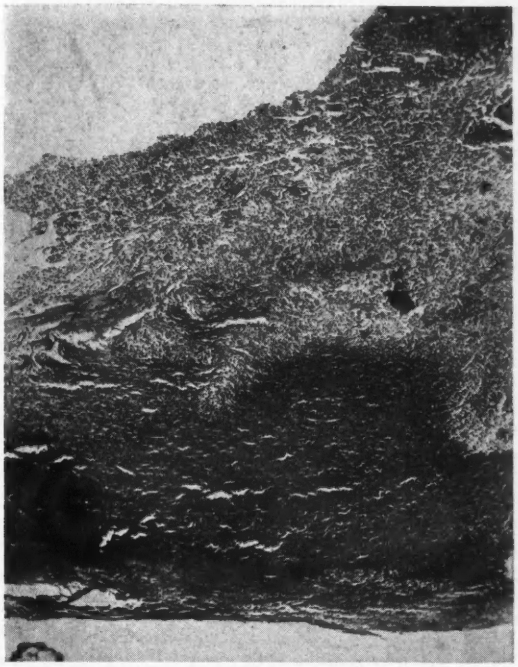

Figure 4.—Aorta. Note the heavy cellular infiltration extending throughout the aortic wall, adventitia (top) to intima (bottom).

hemorrhage may result from direct puncture of a vessel by an ingested object.[4] However, long-delayed hemorrhage as reported by Lascano and Senorans[6] is more compatible with their conclusion that the mechanism is erosion of the esophageal mucosa with subsequent abscess formation and finally aortic perforation following evacuation of the abscess.

Kraus (quoted by Barrie and Townrow) thought the formation of a perivascular clot arrested the initial hemorrhage but that progressive sepsis ruptured this clot, leading to further hemorrhage.

Probably any one or all of the mentioned mechanisms may apply in cases of this type. Since in cases of swallowed bone the offending foreign body is seldom found, it cannot be stated how much of the aortic lesion is due to continued trauma and how much is due to the secondary septic process with no initial direct trauma to the aorta. In the present case the process was probably one of acute localized esophagitis leading to acute mediastinitis and finally periarteritis and arteritis of the thoracic aorta with final weakening of the aortic wall to the point of rupture. No foreign body was recovered and probably the entire course of events was initiated by a superficial wound of the esophageal mucosa without the actual participation of the offending foreign body in the subsequent events. If the perforating object remained in the involved area, it might well be washed out by the gush of blood attendant upon aortic rupture.

Banks,[1] in discussing a similar case, stressed the importance of early esophagoscopy, a view with which the authors are in accord. However, since in several cases esophagoscopy revealed neither the foreign body nor the perforation, and since localized mediastinitis appears to be a major factor in producing aortic perforation with or without aortic-esophageal communication, vigorous chemotherapy is indicated, regardless of the endoscopic findings. Following the swallowing of a foreign body, sequential appearance of initial pain, symptom-free interval, and "signal" hemorrhage should call to mind this syndrome. Probably thoracotomy must be performed if the final fatal hemorrhage is to be prevented.

SUMMARY

A case of aortic-esophageal fistula with fatal hemorrhage secondary to swallowing a fishbone is presented, with clinical and pathological findings. A review of the pertinent literature suggests that localized mediastinitis following esophageal perforation is responsible for the establishment of the aortic-esophageal fistula. Vigorous chemotherapy is imperative even in the face of negative esophagoscopic findings. The sequential appearance of pain, symptom-free interval, and "signal" hemorrhage indicates aortic esophageal hemorrhage and heralds a fatal hemorrhage which may be prevented only by thoracotomy.

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The patient was on the medical service of Lewis Gunther, M.D., College of Medical Evangelists, Los Angeles.

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Term Pregnancy Following Removal of Right Ovary and Left Corpus Luteum Cyst

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THE patient, a 29-year-old white gravida IV, para II, first observed January 10, 1949, reported irregular "spotting" since the last normal menses on September 5, 1948. She also had noted nausea, menstrual-like cramping, low backache, and a pain in the lower left quadrant of the abdomen.

In the three previous pregnancies there had been two normal deliveries at term (1942, 1944) and one spontaneous miscarriage at four months' gestation (1945). In 1945 an appendectomy and a right salpingo-oophorectomy had been done because of an "infection."

Physical findings were within normal limits. Blood pressure was 110 mm. of mercury systolic and 70 mm. diastolic. The uterus was gravid; gestation had progressed approximately two and a half months. There were no palpable adnexal masses. The cervix was bluish and intact. The

hemoglobin value in the blood was 69 per cent. Erythrocytes numbered 3,600,000 and leukocytes 8,200 with normal differential. The blood was Rh-positive, Group O. Result of a Wassermann test was negative. The urine was normal.

The patient continued doing housework, and remained pregnant. She was given iron, calcium and vitamins.

Three weeks later the patient was admitted to hospital in emergency, with complaint of severe cramping in the left side. There was no bleeding. The patient appeared acutely ill, but was not in shock. There was exquisite tenderness in the left adnexal region, where a soft, boggy mass approximately 6 cm. was palpated. This was thought to be either an unruptured ectopic pregnancy or a twisted ovarian cyst.

Under sodium pentothal anesthesia, a midline exploratory incision was made. The size of the uterus was approximately that of a three-month pregnancy, and it was pushed to the right by an ovarian cyst 6 to 8 cm. in diameter. This cyst was twisted 180 degrees upon its pedicle. There was no evidence of a right ovary or tube (previously removed). The cyst was shelled out of its capsule, and approximately one-half of the ovarian tissue was conserved. The pathological diagnosis was corpus luteum cyst. Recovery was uneventful and the patient was dismissed one week later.

For the duration of the pregnancy, increasing doses of stilbestrol were given. The patient complained of frequent cramping and nausea, but at no time was there any bleeding. On August 12, 1949, a normal eight-pound female was delivered by low forceps (used electively) after three hours of labor. Three days later the patient was dismissed from the hospital, afebrile and feeling well.

At examination six weeks postpartum, the uterus was well involuted and in anterior position. The left ovary was of normal size to palpation and was not tender. The cervix was cauterized because of hypertrophy with erosion. Although otherwise she felt well, the patient still complained of some left-side pain. A pyelogram was made; no evidence of disease in the kidneys or ureters was noted.

This case brings up the question of the actual necessity of the corpus luteum hormone in the first trimester of pregnancy. Bonn reported a case in which bilateral oophorectomy was carried out on the 35th day of gestation and pregnancy proceeded uneventfully to term. Hartman stated that, in the monkey, the corpus luteum of pregnancy may be removed as early as the 25th day of gestation without interrupting the pregnancy. Certainly, the answer is not yet known. In the case here reported, stilbestrol was given on the theory that stimulating the secretion of progesterone would reduce the risk of miscarriage. Whether or not the pregnancy would have proceeded to term without it is uncertain.

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Hepatitis and Nephrosis Due to Cough Syrup Containing Chloroform

CHARLES J. WALLACE, M.D., *Sacramento*

IT has been known for over 50 years that chloroform causes damage to the liver, kidneys, heart and nervous system. Instances of poisoning due to chloroform inhalation have been common in years past[1,2] but clinical reports of chloroform poisoning by ingestion are rare[3] and none have appeared in the literature since 1933. Recently an extraordinary case of long-continued daily ingestion of chloroform was observed.

CASE REPORT

A 47-year-old salesman complained of anorexia, loss of libido and generalized weakness of one year's duration. The family history was non-contributory. There had been no major illnesses in the past and the only operation was for repair of a traumatically ruptured testicle during childhood. Chronic sinusitis and bronchitis had been present for 12 years, and several physicians had prescribed Cheracol.®* In traveling about the state the patient visited many physicians and requested prescription for Cheracol. Only the patient was aware of the amount of medicine he used. With some embarrassment, he admitted to an average daily ration of 12 ounces of Cheracol for the past ten years. On occasion, when a particularly bothersome upper respiratory infection occurred, he even increased the daily dose to about 20 ounces. With the 0.8 to 1.3 gm. of codeine thus ingested, the patient also took 1.6 to 2.6 gm. of chloroform daily. Other medication consisted of "One a Day" vitamin pills and occasional use of a penicillin spray. A diet survey revealed an average daily consumption of protein 50 gm., carbohydrate 80 gm., and fat 65 gm. In former years, the patient took one to two whiskey highballs before dinner, but during the past year he had discontinued this altogether because of feeling so "run down."

Upon physical examination the patient was noted to be well developed and well nourished. The weight was 171 pounds, the height 69¼ inches. The patient looked tired. The skin was pale and sallow but not icteric. There was a single spider angioma on the upper back. The odor of the breath was not remarkable. The eyes and ears were normal. The nasal and pharyngeal mucosae were slightly injected and swollen. The tongue appeared normal. Blood pressure, heart and lungs were normal. The abdomen was soft; a smooth, hard, non-tender liver edge extended 9.5 cm. below the xiphoid process and 5 cm. below the mid-clavicular line. The spleen could not be felt. The right testicle was about twice normal size. No abnormalities were noted in a rectal examination. There was no edema in the extremities. The reflexes were normal. Sensation was intact.

Laboratory data: Erythrocytes numbered 3,490,000 with hemoglobin (Dare) 11.0 gm. or 68.8 per cent, giving a color index of 1.0. There was moderate variation of size of red cells, with a moderate number of macrocytic cells. Reticulocytes made up 2.5 per cent of the total. Leukocytes numbered 8,950, with 69 per cent segmented neutrophils, 4 per cent non-segmented neutrophils, 3 per cent eosinophils, 1 per cent basophils, 25 per cent lymphocytes and 3 per cent monocytes. The pH of the urine was 4.0 and the specific gravity 1.018. There was a trace of albumin, no glucose. Many hyaline and granular casts were noted. A very few erythrocytes and leukocytes were observed. A second urine analysis confirmed the trace of albumin and casts. Results of a Kahn test of the blood and of stool examination were

*Each fluid ounce contains 1 grain of codeine phosphate, 2 grains of chloroform, 8 grains of potassium guaicolsulfonate, 8 grains of ammonium chloride, 1/12 grain of antimony and potassium tartrate, alcohol 3 per cent, and white pine and wild cherry bark.

TABLE 1

	January 20, 1949	March 16, 1949	May 21, 1949	July 19, 1949
Erythrocytes Hb.	3,490,000 11.0 gm.	4,050,000 11.6 gm.	4,580,000 14.1 gm.	4,940,000 15.0 gm.
Urine	Numerous hyaline and granular casts per hdf. Trace of albumin.	2 to 3 hyaline and granular casts per hdf. Trace of albumin.	No casts; albumin absent.	No casts; albumin absent.
Bromsulphalein Retention (30 minutes)	14.2 per cent	10.75 per cent	5.5 per cent	5.0 per cent

negative. In a determination of bromsulphalein excretion, using 5 mg. of dye per kilogram of body weight, 14.2 per cent of the substance was retained 30 minutes after administration. The icteric index was 8.8 units. There was 0.85 mg. of total bilirubin per 100 cc. of serum; 47 per cent of it was direct-reacting. Results of two Hanger flocculation tests were normal. Fasting blood urea was 13.4 mg. per 100 cc. The fasting gastric juice contained 14 clinical degrees of free acid. The basal metabolic rate was minus 8. An electrocardiogram was normal. Data of subsequent laboratory procedures during treatment are outlined in Table 1.

Treatment consisted of discontinuing cough syrup and, for a period, substituting codeine tablets, 30 mg. four times a day, and finally stopping these as well. The diet was adjusted to provide protein 90 gm., carbohydrate 200 gm. and fat 75 gm., a total of about 1,800 calories. The patient was permitted to remain ambulatory, but ten hours of sleep per day was recommended.

During the succeeding months, the patient regained normal appetite, strength and libido. Six months after discontinuance of the medicine and institution of the dietary regimen, the patient felt perfectly well; the color of the skin was normal, the spider angioma was gone, and the liver had diminished in size by 2.5 cm. The return of abnormal laboratory findings to normal is shown in Table 1.

SUMMARY

An extraordinary example of chloroform poisoning producing hepatitis and nephrosis is presented. Response to withdrawal of the offending agent and adjustment of the diet to guarantee high protein and vitamin content was gratifying.

2615 Eye Street.

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California MEDICINE

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EDITORIAL

The Doctor Draft

Now that Congress has passed the "doctor draft" bill, medicine can hope for an orderly and equitable solution to the question of who goes first in time of war. Heretofore the question remained unasked and unanswered until emergency was fully upon us and hasty steps had to be taken to solve it.

The bill adopted by the Congress appears to meet with almost complete approval by doctors all over the country. Even before the measure was introduced in the form of legislation, physicians were discussing the advisability of setting up priority classifications where medical officers were needed. As adopted, the bill seems to meet with the popular thinking in medical circles.

There is still much to be learned as to how this measure will work out in actual practice. Selective Service, which is guided by the needs and wishes of the military, must make and interpret numerous regulations. The Army, Navy and Air Force must determine just what their respective needs are and how they may best be met. While these processes are going on, the doctor who may be covered by the law is left in doubt as to his own status. Is the veteran of the Army of the United States still in a reserve status? Is the Navy reserve officer still in reserve? Has the Army terminated its five-year reserve commissions automatically? Is an actual resignation required for a reserve officer to be separated from the reserve?

These are some of the questions which were asked at the recent San Francisco regional meeting of the Council on Emergency Medical Service including top military and Selective Service representatives. Some of them called for technical answers which left just as much confusion in many minds as there had been before. Others brought forth replies which at best could be considered contradictory. The one positive statement that stood out in many minds was the speculation by one military leader that from this time forward every physician should plan to absent himself from his practice for *two* periods of military service. This statement seems as realistic as it is shocking. Present world affairs would indicate the truth of such a conjecture.

In view of this approach to the medical profession by a high-ranking military officer, is it too much to ask that the military services adopt a realistic attitude in their own tables of organization and their use of medical personnel? Many suggestions come to mind and a few might bear investigation.

In the first place, do the military forces need as many physicians as they demand, even in time of war? In the last war, one out of every three physicians was called to duty, a far greater percentage than any other professional, business or working group in the country was called upon to furnish. In many instances these men waited interminably, assigned to specific units which took months to build up. Professionally these doctors got rusty; socially they got bored; economically they got deprived of their normal standard of living while serving as so many "bodies" in a table of organization. Wouldn't it have been better to have had pools of available physicians for assignment to the various theaters of war and to draw upon these pools as medical officers were needed?

Another cause of discord in the medical forces was the overstaffing of many hospitals and dispensaries, resulting in a minimum of work and a maximum of record-keeping and other clerical tasks. A

good corps of non-commissioned and warrant officers could have handled a lot of the paper work and left the doctors free to practice medicine.

Right now we find the Army and Navy treating Veterans Administration patients, as well as dependents of service men. These patients could be cared for by civilian doctors at less cost and with greater convenience to the patient and greater efficiency to the medical corps of the services.

These are a few of the things which might stand a little looking over and a little overhauling. There are others but these stand out as roadblocks in the way of efficient military medical services, in time of war or peace. It would seem that a concerted drive to eliminate these barriers would make the services more attractive to doctors and less disruptive to civilian medical practice.

These criticisms are not new. They have been voiced time and again by civilian doctors who gave up their own careers to serve in the wars in which this country has been engaged. They have been placed before the military leaders for consideration; and, no doubt, some progress has been made in ironing out some of the more noticeable defects. However, in view of the present demand for doctors in what is apparently destined to be a large defense establishment, it looks as though the defense authorities might augment their efforts to clean out the sore spots and make their services more attractive. Medicine has always answered the call, even in numbers out of all proportion to other walks of life; medicine should have some opportunity to ask for a greater efficiency as a means of making the country's medical assets cover the greatest possible ground. That's not too much to ask.

C.M.A. Special Session Cancelled

Several months ago the Council of the California Medical Association voted to schedule a special session of the House of Delegates and selected Sacramento as the site, December 2 and 3 as the dates. At that time it appeared that several items were important enough to warrant the holding of a special meeting for the purpose of discussion as a committee of the whole.

More recently it became apparent that the anticipated discussions were not of such great import as had originally been calculated. Accordingly, the Council decided to cancel the proposed meeting as a means of saving the time, energy and expense involved.

Plans for the Annual Session, to be held in Los Angeles next May 13-16, will permit ample time for the handling of all problems to come before the House of Delegates. Meanwhile, the effort of the December meeting will be eliminated.

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Special Announcement

REGARDING C. M. A. ANNUAL MEETING

To All Members:

The 1951 Annual Session will be held in Los Angeles, Sunday, May 13, to Wednesday, May 16, inclusive. Limited facilities will be available for MOTION PICTURES. If you would like to exhibit send your application to Dr. A. E. Smith, 1930 Wilshire Boulevard, Los Angeles.

PAPERS should be submitted for consideration to the appropriate section secretary (see list on this page).

There will be limited space available for SCIENTIFIC EXHIBITS. If you would like to apply for space, please write immediately to the office of the Association for application blanks. Please indicate space requirements. No exhibit shown in 1950, and no individual who had an exhibit at the 1950 session will be eligible until 1952. No requests for space will be considered after DECEMBER 1, 1950.

All applications for space or program should be transmitted as soon as possible: The deadline is DECEMBER 1, 1950.

ALBERT C. DANIELS, M.D.
Chairman, Committee on Scientific Work

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Information for Authors, Members of Symposia and Panel Discussions

1. Members are reminded that each lantern slide takes approximately one minute for presentation and that *no lantern slide should have more than six lines of text* on it. The interest of the audience is better held by succinct presentation of the principal points.

2. Extra time is *not* allowed for the presentation of slides, movies or other material, except by special arrangement with the section officers *prior to completion of the program.* (Program deadline: *February 1, 1951.*)

3. Authors *must* inform section secretaries *and the Office of the C.M.A.* well in advance of the meeting of any special equipment needed for presentation of papers other than standard lanterns (3½- by 4¼-inch glass slides).

4. The program goes to press in *February.*

MANUSCRIPT INFORMATION

1. All papers are the property of the California Medical Association unless officially released upon *written request* by the author to the Editor of CALIFORNIA MEDICINE.

2. All manuscripts should be submitted in duplicate.

(a) One copy of the manuscript accompanied by an abstract written in *lay language* must be in the office of CALIFORNIA MEDICINE, 450 Sutter Street, San Francisco, at least six weeks prior to the meeting (*by March 31*). This copy will be used to prepare advance material for the press.

(b) Every speaker taking part in the Annual Session should have his final manuscript completed for presentation to the section secretary at the time of delivery of the paper. It should be in proper form for consideration by the Editorial Board of CALIFORNIA MEDICINE.

3. All references must be numbered in alphabetical order, keyed into the text, and in the Table of References must be listed in numerical alphabetical order. (For example: 1. Adams, etc. 2. Brown, etc. 3. Charles, etc. 4. Davis, etc.)

References should follow the style used by the Quarterly Cumulative Index Medicus which is followed by CALIFORNIA MEDICINE: Author's name or names, *Title of the article,* volume and page, *date of publication, including month* and day (if given).

Example:

1. Adams, J., and Smith, J. J.: etc.

2. Brown, J. B., and Fryer, M. P.: Major defects of the face and their surgical repair, Postgrad. Med., 4:420-434, Nov. 1948.

3. Davis, J.: etc.

Industrial Fee Schedule

Summary of the report made by the C.M.A. Industrial Fee Schedule Committee to the Council of the C.M.A., September 9, 1950.

A meeting of the Negotiating Committee and its Advisory Committee was held at the Sir Francis Drake Hotel on January 25, 1950. A general principle was adopted that industrial fees should be based upon a fair rate for effort expended. This does not imply that an industrial case should be handled at a fee lower than one compatible with the cost of ordinary practice. The basic cost of operation of a medical practice has increased as the cost of living has increased in the United States, and there has not been a comparable increase in the fees paid for the care of an industrial patient during the past 20 years. We felt that the whole concept of a fee schedule should be reviewed and reevaluated.

Before entering into any discussion of individual fees, it was felt that the basic relationships between doctors and insurance carriers should be reviewed, and an attempt made to create a closer association between the two groups. The average doctor does not understand the provisions of the California Workmen's Compensation Law as it applies to the practice of medicine and surgery. A summary of the provisions of that law is outlined as follows for the information of doctors who are engaged in practice of this type.

1. *Duty of Employer to Furnish Medical Care:*

Labor Code, Sec. 4600, provides that medical care and hospital treatment "reasonably required to cure or relieve" from the effects of any industrial injury "shall be provided by the employer." The section further provides that in case of the employer's refusal or neglect to provide medical care, the employee may obtain same at the employer's expense. For practical purposes, compensation insurance carriers take over by virtue of their insurance contracts the duty of the employer to furnish medical care, and hence it is the compensation carrier that actually selects and employs the physician.

2. *Provisions Regarding Free Choice:*

Labor Code, Sec. 4600, above summarized, does not provide for any free choice of physician, but on the contrary places the duty on the employer (insurance carrier) to provide both medical and hospital care. *Labor Code, Sec. 4601,* specifies that if the employee requests, "the employer shall tender him one change of physician and shall nominate at least three additional practicing physicians competent to treat the particular case . . . from among whom the employee may choose." *Sec. 4601* specifies that the employee in "any serious case" is entitled to the services of a consulting physician "provided by the employer."

In other words, under our Workmen's Compensation law, free choice of physician is non-existent except for the right of an employee to demand a panel of three from which to choose. In the absence of an employee demand, he must accept the physician selected by the carrier. Even this very limited free choice is further restricted by *Labor Code, Sec. 4603,* that provides that in those instances where the employer maintains for his own employees a hospital and "hospital staff" the employees must accept the physicians on the hospital staff without any right to demand any change.

3. *Selection of Physician by Employee:*

If an employee does exercise his right of free choice and selects a physician other than the ones designated by the insurance carrier, then the services of the physician selected by the employee are at the employee's own expense (*Labor Code, Sec. 4605*).

4. *Medical Examinations:*

The *Labor Code* (*Secs. 4050-4052*) also provides that whenever there has been an industrial injury, the employer (insurance carrier) may require the employee to submit to an examination by a physician selected by the employer, or to an examination by a physician selected by the Industrial Accident Commission or any referee. *Labor Code, Sec. 4055,* provides that any physician who makes an examination, either on behalf of an insurance carrier or the commission or the referee, may be required to report or testify as to the results thereof.

5. *Compensation of Physicians:*

Labor Code, Sec. 5304, provides that whenever there is a dispute between a physician and an employer or insurance carrier with respect to the fees payable for services rendered, the Industrial Accident Commission shall have jurisdiction to settle the controversy "unless an express agreement fixing the amounts to be paid for medical, surgical or hospital treatment . . . has been made between the persons or institutions rendering such treatment and the employer or insurer." In other words, if there is an express agreement between an insurance carrier and a physician, the terms of the agreement control; in the absence of an express agreement, the physician may file a claim with the Industrial Accident Commission, whereupon the commission or a referee, after hearing, may fix the amount payable. In determining controversies between physicians and employers or insurance carriers, the Industrial Accident Commission, or its referees *are not* bound by any particular fee schedule. The law merely provides that the commission, acting as a court, may adjudicate the controversy, and it may apply any fee standard that it sees fit.

6. *Fee Schedules:*

Almost continuously since about 1913 the Industrial Accident Commission has maintained a minimum fee schedule for medical services. These fee schedules have been based on the following legal principle: That the commission has the right to adopt reasonable rules of practice and procedure (*Labor Code, Sec. 5307*); that it has jurisdiction to settle controversies between physicians and insurance carriers over fees (*Labor Code, Sec. 5304*); and that in the exercise of its power to settle controversies it may, under its power to adopt rules of practice, establish a minimum fee schedule as a rule of practice for the *guidance* of its referees. Hence, all minimum fee schedules of the Industrial Accident Commission have been and are merely "rules of practice" for the guidance of referees and the commission itself. There is no provision in our California Compensation Law specifically authorizing or directing the establishment of a medical fee schedule, either minimum or maximum, that would be in and of itself binding in all cases upon everyone concerned. However, as a matter of custom, the Industrial Accident Commission's minimum fee schedules have been adhered to in the main by both insurance carriers and physicians, for the reason that in a disputed case it can be assumed that neither the commission nor a referee would award to a physician a fee below the commission's own minimum schedule.

* * *

The Negotiating Committee of the C.M.A. and the Negotiating Committee of the insurance carriers met in San Francisco on August 24, 1950. The matter of a broad educational program directed towards improving relationships between the medical profession and the insurance carriers was discussed at length. It is planned that a basic outline of instructions is to be published outlining the duties of the attending physician to the insurance carrier, and it is hoped that when this outline is made available some of the criticism on the part of the insurance carriers can be obviated.

Criticism was directed against insurance carriers also, and they have agreed to try to simplify some of their reports in an effort to promote an easier and more simple method of controlling medical care. The insurance carriers have agreed to make a serious effort to condense all reports from all insurance carriers to a single acceptable outline form

and thereby eliminate a good deal of unnecessary secretarial work on the part of the doctors making those reports. A move of this type is surprisingly difficult, and will require time to accomplish. There has been a considerable amount of correspondence regarding the subject of fees to be paid for multiple procedures. The bulk of this correspondence has to do with the practice of charging as separate items an office visit and the injection of penicillin. The attitude of some of the carriers was to the effect that no surcharge was to be paid for the injection of penicillin, and others agreed that the surcharge would be paid on the basis of 50 per cent. They base this compromise decision on Paragraph 5 of the 1950 schedule, which states, "Multiple injuries treated by one physician are to be billed at the greatest fee plus one-half of the fee for the other items." It is our impression that this latter compromise figure will be acceptable to the majority of the insurance carriers billed in that fashion.

The third paragraph of the 1950 schedule, which reads, "To avoid duplication of services when all the required care for a case reasonably falls within the range of qualifications of one physician, no other may claim a fee," was criticized by the doctors. To our amazement, the insurance carriers felt that this paragraph had been most efficacious in eliminating a practice of certain doctors making unwarranted and unnecessary visits to industrial patients. As the insurance carriers bluntly put it, they do not care to be billed for the same thing by two different doctors. They very definitely made it clear that they would never object to the care furnished by two physicians where this care is indicated or necessary. They definitely stated that when medical charges in excess of the schedule are submitted, the insurance company certainly has a right to a reasonable explanation of these excess charges. If a bill of this type includes a reasonable and adequate explanation, insurance carriers are certain it will be given reasonable consideration.

Further meetings of the Advisory Committee of the C.M.A. and of the Negotiating Committee are planned for the immediate future. A revision of a schedule of fees is not going to be simple, nor is it going to be accomplished in any short period of time. We are hopeful that we can, by mutual education of doctors and insurance carriers, arrive at a plan of mutual understanding regarding fees in general. This is the aim of your present committee, and we would appreciate the support and good will of the practicing physicians in the state of California towards accomplishing this end.

FRANK J. COX, M.D., *Chairman*

The California Physician and Civil Defense

JUSTIN J. STEIN, M.D., *Los Angeles*

Chairman, Committee on Emergency Medical Service, California Medical Association; Member, Radiological Safety Advisory Committee; Chairman, Citizens Advisory Committee, Medical and Public Health Services, California Disaster Council

Success in modern war requires total national mobilization of labor, industry, and personnel from the very first intimation of war. We have been indirectly at war for many months, and any hour, day, or month may see the full scale outbreak of hostilities on our own cities, and certainly in the California area. Every nation is vulnerable to attack by a powerful enemy, for a defense against attack is seldom perfect.

Mr. Paul, Larsen, director, Office of Civilian Mobilization, has defined civil defense as follows:

"Civil defense may be defined briefly as the defense of the home front by civilians and civil authority in time of war. It is largely, but not wholly, passive defense.

"For better understanding of the term it is essential to examine in more detail the measures to be employed by civilians and civil authority in their defense of the home front. By so doing, a better appreciation can be had of the importance of civil defense in the total mobilization picture.

"For planning purposes, we have divided the necessary civil defense measures into four groups:

"(1) Measures to avert an enemy attack, such as camouflage, blackouts, aircraft observer systems, and similar quasi-military activities in which civilians may be called upon to assist.

"(2) Advance measures for minimizing the effects of any enemy attack, including such measures as civil air raid warning, the dispersion and relocation of facilities, and the prior evacuation of children and personnel not essential to the war effort.

"(3) Measures to alleviate, control, and repair the damages resulting from enemy attack, ranging from medical and health services, decontamination, and fire fighting, to the removal of debris and salvage.

"(4) And, in connection with the foregoing measures, a group of over-all measures which we

Read in part before the Citizens Medical Advisory Committee to the California Disaster Council, Sacramento, California, July 11, 1950.

term 'general considerations,' such as research and development, legislation, organization, training, policy guidance, military support, and civil defense requirements."[1]

CURRENT CIVIL DEFENSE PLANNING

The summation statement on current civil defense planning, by Paul J. Larsen, at a hearing before the Joint Committee on Atomic Energy, March 30, 1950, is as follows:

"In summation, it can be said that the over-all planning has been basic in order to round out a complete civil defense plan from the Federal Government standpoint, the implementation of which will be the responsibility of the states and local community organizations. Our planning in respect to this Federal Plan has differed from other nations' planning, basically because of our governmental structure and the belief that civil defense operations must be maintained on the basis of our democratic system of government.

"It is our belief that the responsibility of the Federal Government in civil defense activities even after implementation will not require the establishment of a large federal organization in order to insure adequate civil defense to overcome disaster which may occur by enemy action. The federal agency for civil defense will be basically responsible prior to mobilization for (1) formalizing a federal plan which will be accepted by states and local communities, (2) assisting states and local communities in training of volunteer workers, (3) establishing national schools for training of key state and community civil defense personnel, (4) evaluating requirements of equipment and resources for civil defense and determining which of these should be obligations of the Federal Government and/or state and local communities, (5) evaluating weapons effects in order to determine sound dispersion and evacuation policies of government activities and/or other vital installations, (6) maintaining such reserve stores of critical materials as will be required in event of disaster, plus control and distribution of these to communities requiring them in the event of disaster, and (7) maintaining close liaison with the public and public groups through the medium of information, public relations and education on civil defense planning and the dangers which the public should prepare for without introducing hysteria or fear which would affect morale and effective civilian participation in the civil defense program and the public's main functions of maintaining activity at top level for the war effort.

"The national plan can in our estimation be implemented by the states and local communities for the present without necessity for federal civil defense legislation beyond that now existing in the National Security Act of 1947. Additional legislation will be requested when appropriate, in order that the Federal Government can implement its planning, training, and operation program in order to establish supplies for emergency uses and to establish an operating federal organization."[2]

We are therefore dependent upon the National Security Resources Board to present us with an over-all civil defense plan and with proper estimates of the military situation when such estimates are available. The National Security Resources Board will furnish each state with an over-all plan for civil defense in September 1950. This will not be a blueprint, and only basic fundamental suggestions will be made.

WAR AND PEACE-TIME DISASTERS

Differentiation must be made between major disasters occurring in peace-time and those occurring in time of war. For example, in peace-time, major disasters, such as earthquakes, fires, etc., will be handled differently. In peace-time, reserve officers, military personnel and supplies can effectively be utilized, whereas in time of war no military personnel or supplies can be utilized without due regard to the military situation. When plans call for the use of reserve officers and military supplies they should be made with the full realization that the military area commander may prohibit their use because of the existing military situation. It is interesting to note that to date the majority of individuals in California who profess any interest in civil defense are those who witnessed great destruction during World War II in Europe and the South Pacific, and who know that such tragic destruction can very well take place in our cities if we adopt a do-nothing attitude. We cannot stick our heads in the sand like an ostrich and ignore what is happening around us.

TRAGIC MISTAKES BY GERMANY AND JAPAN

The Germans in World War II were repeatedly assured by Goering and others that they had nothing to fear from the standpoint of air bombings. The German cities would be completely protected by the German Air Force. Consequently, very little was done about civil defense planning and organization. The lack of civil defense planning in Germany was disastrous, and when it was begun it was too late. There were 422,000 German civilian deaths, nearly three-fourths of which occurred in the last two years of combat. The number of injured is unknown.[3] Bombing in itself did not result in or foster epidemics there. The Germans, being well trained in personal hygiene, were a bulwark against the breakdown of public health as their cities were being destroyed by the enemy. The Germans had a well organized system for the control, manufacture, and distribution of essential medical supplies.[4] However, they delayed too long in putting their program into effect, and in the curtailment of the numbers and types of dressings, drugs, and of equipment used. One of the first things we must do in the United States is to standardize as much as possible the treatment for various types of injuries and particularly the treatment of burns. Since the percentage of injury by burns will be very high, it can readily be seen that the indiscriminate use of dressings, antibiotics, and blood or plasma would soon deplete the stock-piles unless control is instituted.

In some German cities where civil defense measures were well organized, bombings did not result in complete community disorganization, as was the case in cities where civil defense was not well planned. This was brought out in the comparison of the cities of Duisburg and Hanau. Duisburg was exposed to air raids early in 1941, and a competent and well organized civil defense system gradually grew up in that community. As a result, the casualties were small and essential work was effectively maintained during the period of intense bombings in 1943 and 1944. Hanau, on the other hand, felt that it was too small and unimportant industrially to be a target for heavy air raids, and civil defense plans were not taken very seriously. When a large air raid did occur in December 1944, the Hanau population was panic-stricken and fled the city without organization or plan. Within one night this community of 43,000 people became a mass of ruins, with only five or six thousand people left, and it has never recovered from this disaster.[5]

In Japan these was inadequate planning and organization for civil defense and, again, too late in the war. Many of the casualties from both conventional bombings and from the atomic bombings would have been saved by improved civil defense and first aid measures. Burn cases were very poorly treated and under extremely unhygienic conditions in some areas.

ENGLISH PLANS FOR CIVIL DEFENSE

The English had begun to plan for civil defense in 1935, and an effective highly organized program was well in effect during the early stages of the war. The personnel of civil defense services there reached a peak of 1,900,000 (71.0 per cent males). From a peak of 390,000 full-time males (20 per cent of the total) the number consistently diminished each year after 1941, and the duties of full-time male personnel were assumed by part-time male and female personnel in ever-increasing numbers to June 1944.[6]

Military casualties had to be transported to England from the Continent and treated, medical transport had to be increased, civilian casualties dealt with, and industrial workers under stress kept well and productive.[7] The collection, transport, and first-aid treatment in hospitals of casualties provided excellent lessons for dealing with peace-time accidents and other disasters. Casualties from September 3, 1939, to August 14, 1945, listed by governmental reports, were:

	Killed	Wounded	Total	Ratio Wounded to Killed
Total	357,116	369,267	726,383	1:0.97
Armed Forces	264,443	277,077	541,520	1:0.95
Civilians	60,595	86,182	146,777	1:0.70
Women's Services, Home Guard, Merchant Navy and Fishing Fleets	32,078*	6,008	38,086	1:5.3

*93 per cent in Merchant Navy and Fishing Fleets.

Of the total identified civilians killed, 44 per cent were men, 42 per cent women, and 12 per cent children under 16 years of age. Only 3.9 per cent of the killed and 5.2 per cent of the wounded were civil defense workers on duty. When these figures are contrasted with those from Germany, the excellent results of good civil defense planning are readily apparent.[6]

With only a few minutes' warning a civilian population with an adequate civil defense organization can sustain atomic bombings or conventional air bombings with greatly diminished numbers of casualties. Only a few minutes is required to alert the civil defense organization, for persons to turn off gas, put out hearth fires, and seek shelter.

There have been reports of instances in which persons in Japan saw the atomic bomb coming, immediately took shelter not far distant from the center of the bomb impact, and survived uninjured.

MEDICAL PLANS FOR CIVIL DEFENSE AND MAJOR DISASTER

All local communities should proceed at once to set up a flexible plan which can readily be adapted to any over-all general plan. Even if a general over-all plan is set up, it too will have to be flexible and subject to continuous changes depending upon estimates of the situation.

WHAT CAN THE COUNTY MEDICAL GROUPS DO?

The great success of the civil defense plans in England was the effective efficient working of plans on the local or community levels. The same will be true in future wars. No matter what the national plan, certain fundamental steps must be taken on the local level.

Each county medical group of an appreciable size, and smaller county medical groups, should combine, and appoint at once a committee for civil defense and major disaster. These committees should then do the following:

1. Provide for the procurement and assignment of medical personnel.

The civilian needs for physician services in the next war will be great, probably as great as or greater than the military needs. For this reason attempts should be made to determine the minimum number of physicians required for communities of certain size, taking into account their strategic location. As many combat medical veterans as possible should be retained for the civilian defense set-up. They have been under fire, know how they will react to the initial hysteria, and have been fully indoctrinated into the importance of collection and evacuation of casualties, first-aid measures, treatment of burns, importance of good records, etc. The utilization of medical personnel by the Armed Forces during World War II was very inefficient in numerous instances. *The organized medical profession should at once crystallize its opinions regarding the assignment and procurement of physicians and*

make its recommendations known to the proper authorities. The ordering to active duty of large numbers of physicians when they are not needed is highly demoralizing and poor planning. The civilian medical requirements will be very great in strategic areas such as the San Francisco, Los Angeles, and San Diego areas. These regions have been designated by the National Security Resources Board as probable target areas in California. The organized medical profession must take the initiative in all medical civil defense problems and, as stated above, immediately make known to the Armed Forces its views regarding the procurement and assignment of medical personnel.

Every member of the county medical society or association should be given a certain assignment, and a double check should be made to see that he has not been given too many assignments. If he is on several hospital staffs he should select the one nearest to his home or office and have his name listed for the one assignment plus an alternate assignment in the event he cannot, for some unforeseen reason, go to his original assignment. Female physicians should, of course, be completely incorporated into any medical plan. Disaster identification cards should be given to each physician by his local civil defense committee.

When the assignments are made the reserve status and availability of the physician should be kept in mind.

2. Teams should be organized, teams labeled in accord with their duties: Casualty collecting, blood and blood derivatives, shock, psychiatric and psychologic, radiation casualty, burn, general surgical, maxillofacial, thoracic, vascular, neurosurgical, epidemiological, orthopedic, first-aid, etc.

3. Uniform methods of treatment should be worked out, as much as possible, for burns, radiation injuries, and orthopedic casualties. Many of the casualties will have burn and orthopedic injuries. Supplies should be used sparingly.

4. A simple method of keeping records of all casualties should be established.

5. The number of hospital beds available in the area should be listed: (a) The number of hospital beds in regular use. (b) The number of hospital beds which can be made available for emergency use. (c) The number, capacity, and type of emergency aid stations. (d) Convalescent home facilities, if any. (e) The number of schools, medical buildings and offices, and stores which can be used for aid stations and temporary housing of injured or displaced persons.

6. A survey should be made of transportation available to transport patients or casualties—motor ambulances, motor trucks, motor buses, etc. The number of splints, litters, blankets, and aid kits available should be determined.

It may be necessary to evacuate hospitals or aid stations to other areas.

7. Inventory should be taken of medical supplies in the area concerned, their availability, amount required for normal use. Sources for making up shortages should be listed, and the time required to obtain replacement should be determined.

It would be extremely foolish to stock-pile supplies, such as blood, for example, which is good for only about three weeks. Also the stock-piles, if located in congested areas, could be easily destroyed. It may be necessary to have secret stock-piles to prevent destruction by sabotage.

The types of supplies should be listed as follows: (1) Surgical dressings and bandages. (2) Drugs, biologicals, and antibiotics. (3) Blood and blood derivatives. (4) Surgical instruments and equipment. (5) X-ray supplies and location of x-ray units. Many casualties will require roentgenographic examinations, and outlying offices with x-ray equipment can be used for this purpose for ambulatory casualties. (6) Laboratory supplies. (7) Miscellaneous hospital and medical supplies.

This inventory must include supplies required by hospitals as well as non-hospital supplies.

8. Every hospital should be encouraged to set up a standard operating plan for civil defense and major disaster. Such a plan to prepare for: (1) Evacuation of patients, if necessary. (2) Expansion of present bed facilities on short notice. (3) Selection of alternate hospitals to evacuate to, if necessary. As a part of that plan, the number, location, and capacity of convalescent homes, if any, in the area should be noted. A list should be made of all trained laboratory personnel, registered nurses, practical nurses, nurses' aides, and others who could be immediately called to duty.

SPECIAL PROBLEMS FOR CIVIL DEFENSE

Special problems for civil defense have been considered by the National Security Resources Board[2] as follows:

"*Blood and Blood Derivatives:*

"It has been estimated that several million pints (or units) of blood might be needed within the first few weeks of an attack on our civilian population. Provision of large quantities of this indispensable life-saving item presents some unique problems which arise from the fact that under proper refrigeration, whole blood can be preserved for only three or four weeks.

"Intensive research on methods to extend this period is being conducted, but until it is successful we must base our plans on present limitations. It would be extremely wasteful and probably impossible to maintain a three-week stock-pile of such proportions. Plasma can be kept for several years but, although it is useful in the treatment of shock, it is by no means a complete substitute for whole blood.

"Therefore, the only recourse is a highly efficient organization, including a huge reserve of standard bottles and other supplies, ready to carry out mass

blood procurement from persons outside the attacked area.

"It is entirely possible to devise, on paper, an organization which could recruit millions of blood donors within a period of one to several days. But this is a highly technical operation which produces a commodity that can be lethal unless it is collected and transfused with strict conformity to complex safety standards.

"To activate an adequate and safe war-time blood program without previous, extensive, actual experience in peace-time would be virtually impossible. If an efficient integrated, nationwide peace-time blood program could be organized, it would answer an immense and vital peace-time need and also would offer a strong foundation on which an expanded war-time program could be built with relative ease, safety, and speed. Standardization of equipment is imperative and, in addition, great efforts must be made to extend the period in which whole blood can be preserved and to develop more effective blood substitutes.

"The NSRB, therefore, is initiating a series of conferences between the various interested agencies in order to solve these problems and to plan a blood program which will be adequate for war-time civilian and military needs.

"*Standardization of Supplies for Treatment of Burns.*

"One of the most common types of casualties in civilian war-time disasters is burns. Even before the advent of the atomic bomb, fire raids such as those on Hamburg and Tokyo resulted in enormous numbers of burn casualties. Based on Hiroshima experiences, about 60 per cent of atomic bomb casualties would be burn cases, with or without other accompanying injuries or radiation sickness. It is well known that burns require an extraordinarily large amount of nursing care and supplies. The multiplicity of methods of treatment for burns makes it essential that if reserves of health supplies are developed they must conform to the needs of one uniform system of treatment. We therefore are concentrating a great deal of attention on the development of a method of treatment which would be medically sound and effective and, at the same time. practical for use in large disasters."

SPECIAL TRAINING BY NSRB

Courses to train physicians, nurses, and dentists in the treatment of radiation casualties have already started. Also, courses in radiological monitoring for instruction in the problems of radiological contamination of food, water, and environment in both peace-time and war-time.

A suggested plan of organization of active staff members for hospitals of 50-bed capacity or more for emergency service is as follows:

1. An administrative and evacuation committee. This committee to direct all activities in the hospital and to have charge of evacuation of all patients in the hospital to make room for casualties.

2. Admitting and receiving committee. This committee will admit casualties when necessary, make records of their injuries, and refer to appropriate departments in the hospital.

3. Emergency out-patient committee. All cases needing only emergency out-patient care, as determined by the admitting department, will be treated by this group.

4. Laboratory committee. Emergency blood transfusions, blood counts, etc., will be supervised by this group.

5. Surgical teams to be formed, the number depending upon the size of the hospital staff, and provisions made for their relief.

6. Consultation teams, composed of representatives of the various specialties, such as neurosurgery, orthopedic surgery, urology, radiology, eye, ear, nose and throat, etc., to be available for their services as needed. Special teams for burn cases and radiation injuries should be formed.

7. Hospital care committee. This group to be composed of various specialists and general practitioners to carry out treatment and supervise hospital care of casualties admitted in cooperation with the surgical and consultation teams.

8. First aid teams. Groups of first aid teams can be formed to go out with ambulances to points of disaster to render first aid and determine which patients require hospitalization.

9. Physical hospital committee. Nursing, housekeeping, pharmacy, engineering, laundry, and dietary problems to be supervised by this committee. This committee will plan for the procurement, storage, issue, replenishment, repair and maintenance of hospital plant facilities, medical equipment and supplies, patients' food supplies, and medical transportation.

THE C.M.A. EMERGENCY MEDICAL SERVICE COMMITTEE

1. This committee will encourage and assist wherever possible the local county medical groups in their planning for civil defense and major disaster. Suggestions have been made to that end in this paper. The medical profession must take the initiative and have workable plans. We shall not wait for some government agency to do it for us.

2. The California Medical Association is represented on the Medical Advisory Committee of the Disaster Council for the State of California and on the Radiological Safety Advisory Committee.

3. This committee will help coordinate the medical activities of the local county medical groups and the C.M.A. with that of volunteer agencies, city and state health departments, the military, and the National Security Resources Board.

4. As quickly as it is received, any information of value regarding civil defense will be passed on to the local county medical civil defense committees. An enlightened medical profession and public will always react more favorably in the event of a crisis.

5. We must justify the public confidence, as physicians have always done in the past, by consistently increasing our knowledge of the care and maintenance of the sick and injured in the event of enemy attacks.

LEGISLATION FOR CIVIL DEFENSE IN CALIFORNIA

California has a disaster act[8] which was amended at the 1945 session of the Legislature. Article 1, paragraph 1500, reads as follows:

"The State has long recognized its responsibility to provide for preparedness against disasters that may result from such calamities as flood, fire, earthquake, pestilence, war, sabotage and riot. It is hereby found and declared that it is necessary, to enable the State to more effectively join with political subdivisions, municipal corporations and other public agencies of the State, in preparing to cope with and guard against conditions which may result in extreme peril to life, property and the resources of the State and generally to protect the health and safety and preserve the lives and property of the people of the State, and in times when the United States of America is engaged in war, to assist the Federal Government in the successful prosecution thereof, that a readjustment of the provisions of law for dealing with such hazards be accomplished in the light of war-time experience, and that advantage be taken of those implements and methods, organizations and arrangements that have already been developed to deal with possible future disasters."

Article 3, paragraph 1520, entitled Citizens' Advisory Committees, is as follows:

"The Governor may create advisory committees to assist in specific fields of civilian protection, war services and disaster preparedness. He shall appoint members thereof and they shall serve at his pleasure. He shall also designate the chairman and vice-chairman thereof. The committees shall be under the direction of the Governor or such State department head as he shall designate, and shall be wholly advisory in character and shall not be delegated any administrative authority or responsibility. Members of such committees shall not receive compensation from the State for their services under this chapter, but when called into conference or session by the Governor or a department head designated by him shall be reimbursed for their actual and necessary expenses incurred in connection with such conferences or sessions, or in lieu thereof shall receive mileage and ten dollars ($10) per day of actual service."

The Governor has appointed the Medical Director of the State Public Health Department to act as chairman of the Medical Advisory Committee and to direct all medical activities. He has also appointed Dr. Justin J. Stein, chairman of the Emergency Service Committee for the California Medical Association, to be a member of this Citizens' Advisory Committee.

NEEDED LEGISLATION

No provision is made in the California Disaster Act to cover professional licenses while working under mutual aid agreements with neighboring states under civil defense. Provision should be made in the act for the temporary licensure coverage of California physicians working in Nevada and Arizona, or any other state, in the event of a grave civil emergency. Also, provisions should be made to provide for the coverage of injuries or sickness compensation to physicians while engaged in such work. Provisions to provide compensation for injuries while working as civil defense workers in California have already been enacted. Recommendations to cover the above have already been made to Governor Warren by Paul Larsen and the Citizens' Medical Advisory Committee on July 12, 1950.

ATOMIC, BIOLOGICAL, AND CHEMICAL WARFARE

Atomic Warfare.

Dr. Charles L. Dunham, of the Atomic Energy Commission, has expressed his views as follows:[9] "I should like to emphasize my own personal view on the importance of keeping a proper perspective in civil defense activities. The atom bomb has added a new factor to be reckoned with in modern warfare, but it is not sound thinking to over-emphasize the role atomic energy will play in any future war to the exclusion of planning for emergency medical support against conventional block busters and fire bombs or such conventional forms of warfare as bacteriological and poison gas."

We should plan for atomic bomb warfare. An atomic bomb detonated in the air over a large city will probably do the following:

1. Knock out 60 per cent of the hospital bed capacity and a large percentage of medical personnel in the area.

2. Destroy 40 per cent of the fire fighting equipment.

3. Cause electric power failures and shortages of water supply, food and shelter.

4. Necessitate care for thousands of casualties and the evacuation of casualties to areas 40 or more miles away from the area.

Mutual aid agreements with non-involved areas must also be planned. If a good workable civil defense plan is in operation with mutual aid agreements, the number of casualties from atomic bombings can be greatly reduced.

Considerable data regarding atomic warfare will be furnished to California physicians in the near future.

Biological Warfare.

In September 1950 the National Security Resources Board presented all available non-classified data regarding biological warfare to the various states. This means of warfare may be used by saboteurs prior to an attack. Good sanitation and special

emphasis upon public health precautions will reduce the hazards of warfare of this type.

It will be necessary for civilians to report unusual sickness of themselves and any of their domestic animals to physicians who, in turn, can carry out proper reporting of such diseases.

Civilians should be encouraged to seek advice and information from their physicians regarding any unusual sickness of humans, plants, or animals. The Public Health, Veterinary, and Agricultural services have been advised to be aware of the possibilities of biological warfare.

Chemical Warfare.

Data regarding chemical warfare are to be made available to all state civil defense groups.

CONCLUSION

All local medical components of the California Medical Association should at once appoint civil defense committees. These committees are to proceed rapidly in organizing the medical personnel and hospitals in their areas. The slogan "It is later than you think" should be adopted.

The organized medical profession must take the initiative in medical civil defense planning. Civil defense is here to stay. Effective local planning is the most important step to insure success in time of disaster.

1407 South Hope Street.

REFERENCES

1. Quoted by George M. Lyon, M.D., in lecture entitled "A Suggested Civil Defense Organization," given April 6, 1950, at University of California at Los Angeles.

2. Civil Defense Against Atomic Attack. Hearing before Joint Committee on Atomic Energy and 81st Congress of the U. S., March 30, 1950. U. S. Government Printing Office, Washington, D. C., 1950.

3. The Effect of Bombing on Health and Medical Care in Germany. U. S. Strategic Bombing Survey, U. S. Government Printing Office, Washington, D. C., 1950.

4. Quoted by Colonel William L. Wilson, M.C., U.S.A. How Should We Apply These Lessons Learned in World War II to Future Planning? (Data to be published.)

5. Hearing before the Joint Committee on Atomic Energy and 81st Congress of the U. S. on Civil Defense Against Atomic Attack. Part 2, March 30, 1950. U. S. Government Printing Office, Washington, D. C., 1950.

6. The Prime Minister and the Minister of Defense: Strength and Casualties of the Armed Forces and Auxiliary Services of the United Kingdom 1939 to 1945, London, H.M.S.O. (Cmd. 6832), 1946.

7. Quoted by Colonel William L. Wilson. (See Reference 4.)

8. California Disaster Act. Earl Warren, Governor, California State Printing Office.

9. Statement prepared by Dr. Charles L. Dunham, Chief, Medical Branch, Division of Biology and Medicine, A.E.C., for meeting of Council on National Emergency Medical Service of A.M.A., May 6, 1950.

* * *

NOTE: Colonel William L. Wilson, M.C., U.S.A., in office of the Surgeon General of the Army, Washington, D. C., has written numerous excellent articles on civil defense for those interested in this subject.

In Memoriam

BEATTIE, WILLIAM A. Died in Penryn, September 5, 1950, aged 69, in an automobile accident. Graduate of Cooper Medical College, San Francisco, 1912. Licensed in California in 1912. Dr. Beattie was a member of the Sacramento Society for Medical Improvement, the California Medical Association, and the American Medical Association.

✤

CROOKS, SAMUEL A. Died in Loma Linda, September 2, 1950, aged 58, of coronary thrombosis. Graduate of the College of Medical Evangelists, Loma Linda-Los Angeles, 1927. Licensed in California in 1929. Dr. Crooks was a member of the San Bernardino County Medical Society, the California Medical Association, and a Fellow of the American Medical Association.

✤

GEORGE, WILLIAM A. Died in Loma Linda, September 4, 1950, aged 84, of cerebral arteriosclerosis. Graduate of the University of Michigan Medical School, Ann Arbor, 1894. Licensed in California in 1911. Dr. George was a retired member of the San Bernardino County Medical Society, and the California Medical Association.

✤

JAMES, CHARLES S. Died in Fairfield, Iowa, September 11, 1950, aged 79. Graduate of the University Medical College of Kansas City, Mo., 1891. Licensed in California in 1924. Dr. James was a retired member of the Los Angeles County Medical Association, the California Medical Association, and a Fellow of the American Medical Association.

✤

KAHN, MAURICE G. Died in Los Angeles, September 12, 1950, aged 77, of a coronary. Graduate of Harvard Medical School, Boston, 1898. Licensed in California in 1914. Dr. Kahn was a member of the Los Angeles County Medical Association, the California Medical Association, and a Fellow of the American Medical Association.

✤

LOW, TRIUMPH C. Died in Los Angeles, September 17, 1950, aged 78. Graduate of the Chicago Homeopathic Medical College, 1897. Licensed in California in 1900. Dr. Low was a member of the Los Angeles County Medical Association, a life member of the California Medical Association, and a Fellow of the American Medical Association.

✤

MCCOY, EARL T. Died in Los Angeles, September 14, 1950, aged 66, of coronary thrombosis. Graduate of the College of Physicians and Surgeons, Los Angeles, 1918. Licensed in California in 1918. Dr. McCoy was a member of the Los Angeles County Medical Association, the California Medical Association, and the American Medical Association.

McGRAW, HARRIET G. KURTZ. Died in San Bernardino, June 5, 1950, aged 59, of carcinoma of the pancreas. Graduate of Bennett Medical College, Chicago, 1907. Licensed in California in 1917. Dr. McGraw was a member of the San Bernardino County Medical Society, the California Medical Association, and a Fellow of the American Medical Association.

✤

MACCRACKEN, WILLIAM B. Died in Piedmont, September 14, 1950, aged 81, after a long illness. Graduate of New York University Medical College, 1893. Licensed in California in 1911. Dr. MacCracken was a retired member of the Alameda County Medical Association, and the California Medical Association.

✤

SHUMATE, FREDERICK O. Died in New York City, August 8, 1950, aged 49, of myosarcoma—metastatic to lung (from scar on leg). Graduate of Northwestern University Medical School, Chicago, 1931. Licensed in California in 1931. Dr. Shumate was a member of the San Francisco County Medical Society, the California Medical Association, and a Fellow of the American Medical Association.

TERRY, WALLACE I. Died in San Francisco, September 22, 1950, aged 81, of diverticulitis, sigmoid colon. Graduate of the University of California Medical School, Berkeley-San Francisco, 1892. Licensed in California in 1893. Dr. Terry was a retired member of the San Francisco County Medical Society, and the California Medical Association.

✤

TWITCHELL, EDWARD W. Died in San Francisco, September 3, 1950, aged 79. Graduate of Cooper Medical College, San Francisco, 1892. Licensed in California in 1893. Dr. Twitchell was a retired member of the San Francisco County Medical Society, and the California Medical Association.

✤

WALLACE, WILLIAM S. Died in Las Vegas, Nevada, September 15, 1950, aged 81, of coronary thrombosis. Graduate of Jefferson Medical College of Philadelphia, 1893. Licensed in California in 1920. Dr. Wallace was a retired member of the Orange County Medical Association, the California Medical Association, and an Associate Fellow of the American Medical Association.

Questions and Answers about C. P. S.

Question: **Under the Veterans' Program, is it permissible to charge veterans in addition to the fees paid by C.P.S.-VA?**

Answer: No. The payment for medical services rendered for authorized treatment is payment in full for such services. The veteran may not be charged in excess of the fees allowed under the C.P.S.-VA program.

However, when a veteran is being treated for more than one condition, only one of which is service-connected, the doctor may charge the veteran his usual fee for treatment of the non-service connected condition.

Question: **Will the Veterans' Program authorize me to perform an examination requested by a veteran for pension purposes?**

Answer: No, unless specifically authorized by the Veterans Administration. Any examination requested by the veteran to be used in prosecuting his claim for compensation must be paid for by him as a private patient.

Question: **How does C.P.S. establish fees for removal of tumors, inasmuch as the fee schedule indicates a range of unit values for these procedures?**

Answer: Several factors are considered in establishing C.P.S. fees for removal of tumors. These factors include the location and size of the tumor, whether it is malignant or benign, difficulties encountered in its removal, and the time required for the excision. The doctor should always provide this information on bills submitted to C.P.S. This will avoid incorrect payment and delay in processing the claim while C.P.S. contacts the physician for additional information.

Question: **Are preoperative surgical consultations covered by the C.P.S. Surgical Contract?**

Answer: C.P.S. liability under the Surgical Contract begins at the time of surgery. Therefore, *preoperative* care (such as consultations and examinations) are not benefits of the Surgical Contract. This care is considered to be medical care and thus only payable by C.P.S. when the member has medical benefits which apply.

Question: **Is it true that dependents of C.P.S. members enrolled through C.S.E.A. now have medical-service-while-hospitalized?**

Answer: Yes, in a large number of cases. In the past the C.S.E.A. contract provided surgical, hospital and two-visit-deductible medical benefits for the subscriber, and surgical-hospital for family dependents. Recently medical-service-while-hospitalized was offered to the family dependents, and approximately 10,000 have now added these benefits to their existing surgical-hospital coverage. All these persons have been issued new C.P.S. identification cards which show that they have medical-service-while-hospitalized protection. C.S.E.A. dependents who have not availed themselves of the supplementary benefits retain their old identification cards.

Question: **If I have a C.P.S. case which I believe is payable under Workmen's Compensation, do I bill both Workmen's Compensation and C.P.S.?**

Answer: No. Bill Workmen's Compensation; if payment is rejected, then bill C.P.S., indicating the reason for rejection by Workmen's Compensation. C.P.S. will make payment if the services rendered are benefits of the member's contract. If it appears that litigation will delay settlement by Workmen's Compensation, be certain to notify C.P.S. within six months from date of services so that if the insurance carrier does not pay the claim, it can still be paid by C.P.S.

Question: **What is the difference between Blue Cross and Blue Shield?**

Answer: Blue Cross is the association of hospital-sponsored non-profit hospitalization plans throughout the nation. Blue Shield is the national association of doctor-sponsored medical and surgical plans. California Physicians' Service is the Blue Shield plan in California.

In Southern California, C.P.S. has operated jointly with Blue Cross for many years. As of August 1, 1950, this joint relationship was terminated. Each now operates independently, and C.P.S.-Blue Shield now offers to the public a hospitalization contract in addition to its surgical and medical programs.

Thus, since an increasing number of C.P.S.-Blue Shield patients in Southern California will have C.P.S. hospitalization, it is more than ever important for doctors and their nurses and secretaries to examine patients' identification cards to determine if the hospitalization is provided by C.P.S.-Blue Shield or Blue Cross.

Question: **Why is it that bills I send to the Veterans' Program about the middle of any given month are not paid as quickly as those I send in around the first of the month?**

Answer: Requests for reauthorization are processed by the Veterans' Program between the 20th and 30th of each month. Any bills received during this period require special handling. The normal period for processing bills is between the first and 20th of the month. Therefore, bills on Form 53 which are received between the first and 15th of each month are handled more rapidly than those received during the latter part of the month.

NEWS and NOTES

NATIONAL • STATE • COUNTY

LOS ANGELES

Seven appointments to the faculty of the University of California at Los Angeles School of Medicine were approved last month by the regents of the university. The appointees are: Dr. Lowell S. Goin, clinical professor of radiology; Dr. Horace W. Magoun, professor of anatomy; Dr. Robert Mazet, associate clinical professor of surgery; Dr. Daniel G. Morton, professor of obstetrics and gynecology; Dr. Claude S. Mumma, associate clinical professor of surgery; Dr. Neville H. Rupp, assistant clinical professor of surgery, and Dr. David H. Sprong, associate clinical professor of surgery.

* * *

Dr. Byron O. Mork, Jr., recently was appointed district health officer for the Hollywood-Wilshire district, with headquarters at 1456 North Bronson. In this post with the City of Los Angeles department of health he succeeds Dr. Monroe Epstein who was acting district health officer for Hollywood-Wilshire and who is in charge of the northeast district as part-time district health officer.

* * *

The third annual midwinter **radiological conference** sponsored by the Los Angeles Radiological Society will be held at the Biltmore Hotel, Los Angeles, February 24 and 25, 1951. The cost for the two-day session is $15. A banquet will be held on Saturday evening, February 25, at which the guest speaker will be Dr. Edward Chamberlain, professor and chairman of the department of radiology, Temple University, Philadelphia. A second out-of-state speaker at the conference will be Dr. Edward B. D. Neuhauser, roentgenologist, Infants and Children's Hospital, Boston. The fee for the banquet will be $5. Reservation for the conference and banquet should be accompanied by a check for $20 and sent to Dr. John B. Hamilton, 210 North Central Avenue, Glendale 3, California.

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The Los Angeles Urologic Society has announced that the fourth **urologic postgraduate seminar** will be held at the Ambassador Hotel, Los Angeles, November 27 to December 1, 1950. The seminar is sponsored by the American Urological Association and by the western branch of the association. The course is designed, the announcement said, "primarily to cover recent developments in urology, including the outstanding contributions in research as well as those in the surgical field. Basic science courses related to urology will be emphasized."

Fee for the course will be $60, which includes tuition, banquet and luncheons. Certificates of eligibility for veterans will be processed by the College of Medical Evangelists.

Further information may be obtained from Dr. Tracy O. Powell, secretary, Suite 915, 6253 Hollywood Boulevard, Los Angeles, 28.

SAN FRANCISCO

Dr. Anthony J. J. Rourke, superintendent of Stanford Hospitals, was elected president-elect of the American Hospital Association at the recent annual meeting of that organization in Atlantic City.

An $81,000 **grant by the National Heart Institute** was awarded last month to the University of California in support of research on fundamental biochemical and biophysical factors in the pathogenesis of atherosclerosis. The research project is under the direction of Dr. John W. Gofman.

SANTA CLARA

An advertising campaign by the Santa Clara County Medical Society to acquaint the public with its views on medical questions has been acclaimed by the Bureau of Advertising, American Newspaper Publishers Association, as one of the **outstanding advertising performances** of 1949. The society's advertising project was one of 50 campaigns chosen from hundreds of entries for inclusion in the 1950 edition of "The Blue Book of Newspaper Advertising." The campaign was a series of ads, each expounding some phase of the society's policies regarding free medical care, fees for medical services, and the benefits of voluntary as compared with compulsory health insurance.

Within a short time after the start of the advertising campaign, hundreds of inquiries were received for information on the availability and benefits of voluntary health insurance in the area. Numerous comments came in from social service organizations, public health officials, nurses and welfare department employees, all commending the society for establishing such clear-cut policies and for making them known to the public.

YOLO

Dr. Roy A. Neumann has been appointed county physician of Yolo County to succeed Dr. Frank Peter who resigned to enter private practice.

GENERAL

More than 2,000 medical specialists in x-ray and radium from every state in the Union are expected to attend the 36th annual meeting of the **Radiological Society of North America,** which will be held in Chicago at the Palmer House, December 10 to 15, according to announcement by that organization. The opening program on Monday morning will deal with a discussion of economic problems in the field of radiology.

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The ninth annual meeting of the **American Academy of Dermatology and Syphilology** will be held in Chicago from Saturday, December 2, through Thursday, December 7.

The principal sessions will be held at the Palmer House, with special courses in histopathology and mycology scheduled for Saturday and Sunday, December 2 and 3, at the medical schools of the University of Illinois and Northwestern. Special courses in x-ray and radium therapy and bacteriology of the skin will be held Saturday and Sunday at the Palmer House. There will also be special courses in anatomy and embryology of the skin and special problems in dermatohistopathology Sunday at the Palmer House.

Physician-members of **California Physicians' Service** have been paid $7,652,403 for medical treatment rendered to veterans since inauguration in 1946 of the Home Town Care Program, according to a study recently completed by the C.P.S. veterans' department.

The study gives the following breakdown of payments:

April 1, 1946 to March 31, 1947	$1,425,191
April 1, 1947 to March 31, 1948	1,741,789
April 1, 1948 to March 31, 1949	1,840,424
April 1, 1949 to March 31, 1950	2,159,501
April 1, 1950 to June 30, 1950	485,000

Also revealed by the study was that during the first nine months of 1949 more money was paid to California doctors under the C.P.S.-VA program than the combined payments under all other Blue Shield programs where the health plan acts as an "intermediary" between VA and veterans. In that period C.P.S. physician-members received $1,614,549; doctors in the seven other intermediary plans received $901,467.

Other facts brought out by the survey include:

1. A tabulation in March 1950 showed 5,255 C.P.S. physician-members had one or more veterans under treatment.

2. Approximately 62,500 California veterans have been treated under the C.P.S.-VA program during the three years of 1947-1950.

The study also revealed a notable **reduction in administrative costs.** In 1947, 130 employees (both C.P.S. and VA) were producing an average of 7,500 authorizations for treatment per month. Currently, only 97 employees are required to produce an average of 11,000 authorizations per month.

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The American Dermatological Association is offering a **prize of $300 for the best essay** submitted on original work, not previously published, relative to some fundamental aspect of dermatology or syphilology. Manuscripts should be sent not later than February 1, 1950, to Dr. Louis A. Brunsting, secretary, American Dermatological Association, 102-110 Second Avenue, Southwest, Rochester, Minn.

Competition is open to scientists generally; not necessarily physicians.

The prize winner may be invited to present his paper before the annual meeting of the American Dermatological Association which will be held May 23 to 26, 1951, at Hot Springs, Virginia.

Federal and state financial aid will help construct **nine hospital and health center facilities** in California in the 1950-51 fiscal year, but tentative allocations to 11 other projects have been rescinded due to a 50 per cent reduction in federal funds available for the hospital construction program, the State Department of Public Health announced recently.

Projects **approved for allocation** this fiscal year include seven health centers and two hospitals, the Health Department said. They are: San Benito County Health Center, Hollister; Madera County Health Center, Madera; Kings County Health Center, Hanford; San Luis Obispo County Health Center, San Luis Obispo; Butte County Health Center, Oroville; Santa Clara County Health Center, San Jose; Los Angeles City Health Center (Westchester District), Los Angeles; St. Joseph's Hospital, Eureka—75-bed new hospital facility; Centinela Valley Community Hospital, Inglewood—48-bed addition.

Projects from which it was **necessary to withdraw financial assistance** are: Daniel Freeman Memorial Hospital, Inglewood; Pittsburg Community Hospital District, Pittsburg; St. Augustine-West View Hospital, Los Angeles; San Diego Memorial Hospital, San Diego; Fresno County Hospital, Fresno; Del Norte County Local Hospital District, Crescent City; Rancho Los Amigos, Hondo; Herrick Memorial Hospital, Berkeley; San Bernardino City Health Center, San Bernardino; San Jose Public Health Center, San Jose; and Orange County Health Center, Santa Ana.

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The fifth congress of the **Pan-Pacific Surgical Association** will be held in Honolulu November 10 to 21, 1951.

"The object of the Pan-Pacific Surgical Association," according to the official announcement of the meeting, "is to bring together surgeons from countries bordering on the Pacific Ocean so as to permit the exchange of surgical ideas and methods and to develop a spirit of good fellowship among the various races represented. Although it was planned that meetings would be held every three years, world events have permitted but four conferences since the organization was conceived—the first in 1929 and the last in 1948."

Further information may be obtained by writing the Pan-Pacific Surgical Association office, Suite 7, Young Building, Honolulu, T. H.

BOOK REVIEWS

DIE HAUTTUBERKULOSE UND IHRE THERAPIE. By Prof. Dr. Gustav Riehl and Dr. Oswald Kopf. Verlag Wilhelm Maudrich, Wien—1950.

This book, in German, is an excellent summary of our knowledge of cutaneous tuberculosis and particularly of its successful treatment with vitamin D_2. The authors are particularly qualified to speak on this subject as they have a wealth of clinical material upon which to draw. One can see as many cases of cutaneous tuberculosis in a day's visit to the Lupus Heilstat and the Wilhelminenspital in Vienna as he would see in a lifetime in dermatology in California.

After a general review of the subject, with excellent clinical photographs, the authors take up in detail the treatment which has done so much to conquer this disease, namely vitamin D_2. The "before and after" photographs show the good results of treatment. Other forms of therapy such as Finsen-Lomholt lamp therapy, tuberculin, local applications and surgery are well covered.

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BRIDGES FOOD AND BEVERAGE ANALYSIS. By Marjorie R. Mattice, A.B., Sc.M., Assistant Professor of Biochemistry, Graduate School of Medicine, College of Medical Evangelists, Los Angeles. Third Edition, Thoroughly Revised. Lea and Febiger, Philadelphia, 1950. $5.50.

This is probably the most comprehensive reference of its kind available to the physician. It presents under one cover a great abundance of data convenient for answering specific inquiries about the values of foods. However, it has several disadvantages: To begin with, it buries in its almost 400 pages the complete picture of any one food. This defect is especially apparent to the student and dietitian who must plan a diet embracing vitamins and minerals as well as nutritive and caloric values. There is also a considerable inconsistency in emphasis: For example, the acidity and alkalinity tables are presented in great detail, whereas there is brief treatment for the cholesterol and amino acid contents of food. No tables of ideal weights for adults are given. Tables 8 and 9 (of average weights for men and women) are misleading to the student and ignore the fact that the average weight of older American adults is far above the ideal and that the mortality is correspondingly higher. The calcium and oxalic table of foods could be benefited by adding a footnote for comparing the percentage of calcium in milk and cheese. While many common "brand" foods are included, there are many, equally common, omitted (e.g., Triscuit, Monterey Jack cheese, chewing gum, etc.).

It seems too bad that there is such a variation in the values for the same food as given by different authorities in the nutritional field. It is also too bad that an authority such as this one should give contradictory values for the same food. For instance, on page 81, a 50 gm. egg is listed as having 6.7 gm. of protein, 5.2 gm. of fat and 75 calories, whereas a 50 gm. *poached* egg is listed as having 6.2 gm. of protein, 5.8 gm. of fat and 80 calories. Perhaps the figures were compiled from different investigators at different times and were not studied by the compiler.

For a future edition of this volume, the reviewer suggests that the principal tables be divided into groups of foods (such as cereals, milk, meats and legumes) with as complete a picture as possible of the food composition including carbohydrates, proteins, fats, minerals, vitamins, acidity and alkalinity, cholesterol, amino acids and calories.

Despite these various criticisms, the book is still recommended as being as good a reference as one can find in its field.

PROCTOLOGY IN GENERAL PRACTICE. By J. Peerman Nesselrod, B.S., M.S., M.Sc. (Med.) M.D., F.A.C.S., F.A.P.S., Associate in Surgery, Northwestern University Medical School. Illustrated. W. B. Saunders Company, Philadelphia, 1950. $6.00.

This is a highly personalized book. The author gives an account of his own ideas, experiences and practice; he details just how he works to a much greater extent than is found in the average medical text. As one is guided through the various chapters, which include the fundamental anatomy and physiology, diagnostic procedures and disease conditions of the anus and rectum, one feels much more than usual that the author is personally standing over his shoulder. The illustrations are well done and explicit; the paper and printing are good.

The use of the book, as its title implies, is primarily for the general practitioner who wishes to do diagnostic or operative proctology. It is a sound and practical manual which can be readily recommended.

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HUMAN STERILIZATION TECHNIQUES OF PERMANENT CONCEPTION CONTROL. By Robert Latou Dickinson, M.D., and Clarence James Gamble, M.D. May be ordered from Planned Parenthood Federation of America, 501 Madison Ave., New York 22, N. Y. 1950.

This is an attractively gotten-up brochure on the subject of sterilization. It discusses the possible reasons for the procedure, the commonly employed techniques, the efficiency of these techniques, and the implications. It is well illustrated by line drawings. Under indications are included mental deficiency, certain cases of mental disease and of epilepsy, and inheritable diseases which kill, cripple, or severely handicap. Also included are conditions which have necessitated an excessive quota of cesarean sections, diseases of the heart, lungs or kidneys which make pregnancy hazardous, excessive number of children or enfeebled health which render further pregnancy an unwarrantable risk, mental illness which causes child care to constitute a serious complication, mental deficiency and psychosis which interfere with the proper upbringing of potential children, and the circumstance in which "a man and wife have produced all the children they can rear with health, happiness and usefulness for progeny and parents."

Anatomy and techniques are described for both male and female. The illustrations make this section clear even to the uninitiated. The authors appear to favor the Pomeroy technique. The small and decreasing percentage of failures is remarked.

One section is devoted to the thesis that the usual techniques, involving the interruption of the continuity of the Fallopian tubes in the female, and of the vas deferens in the male do not interfere with sexual function, an idea often held erroneously. The authors wish to disabuse the public of the idea that sterilization (by the technique mentioned) means castration.

The reviewer fails to comprehend the intention of the brochure. Its language and format suggest that it is intended for the laity; if so, the sections dealing with technique are needlessly detailed and contain words not easily understood by this group. If the brochure is for the profession, it is incomplete.

The authors' philosophy appears to be eugenically sound but how widely accepted it will be cannot be said. Certainly not everyone will approve of many of the indications espoused by the authors.

PLASTIC AND RECONSTRUCTIVE SURGERY — A Manual of Management. By Ferris Smith, M.D., F.A.C.S., Consultant in Plastic Surgery, Blodgett Memorial Hospital, Grand Rapids, Michigan. W. B. Saunders Company, Philadelphia, 1950. $15.00.

In a 900-page work, Dr. Ferris Smith of Grand Rapids, Mich., has summarized the experience of his 35 years of plastic surgical practice in a form which is both readily useful and dogmatic in detail for any given surgical procedure. The book is well set up and well illustrated and reviews many accepted procedures in the treatment of congenital and acquired deformities of the head and neck, as well as grafting of burns, and some peripheral plastic operations.

Dr. Smith, who is one of the great pioneers in plastic surgical teaching in the United States, stresses again and again the importance of using local tissue rather than skin-grafts on exposed surfaces of the head and neck. This is a most worthwhile principle and should be followed wherever possible. His techniques of multiple excision and Z-plasty are very useful but are emphasized to the point of overdoing them, particularly as regards the extremities.

The procedures illustrated are for the most part satisfactory and are good standard practice in plastic surgery. On the other hand, some procedures recommended seem unnecessarily complicated with many steps which accomplish little in the way of end result. Particularly notable is a many-staged procedure for total eyelid reconstruction in which other surgeons might feel that obliteration of the socket altogether would give a more satisfactory end result without the tedium of so many operations.

The broader aspects of plastic surgery, which include the care and treatment of carcinoma of the head and neck and its resulting defects, reconstructive surgery of the hand, lower extremity surgery, genito-urinary and gynecologic plastic surgery and some other fields, are covered very lightly in this manual, and one must seek other texts for authoritative procedures if one is to have a well-rounded authority on all phases of the specialty. In defense of this limitation of the text, Dr. Smith states in the preface that "There are many borderline cases occurring in general, genito-urinary and orthopedic surgery, dermatology, etc. It is the author's belief that such conditions as hypospadias and epispadias and the like should be corrected by the urological surgeons, absence of the vaginal tract by the gynecologist, many of the lesions of the tendons, nerves and bones of the hand and feet by an orthopedist." With this, most plastic surgeons will not agree, as the broad general surgical background of modern plastic surgery encompasses many fields which overlap other special fields of endeavor, and the plastic surgeon would feel his prolonged training in various fields to be of limited value if confined to head and neck and surface lesions.

This book is of value both to the medical student and to the interested surgeon in related specialties as well as to the plastic surgeon. It provides, however, but one man's point of view and should be supplemented by reading and experience with other authors for a well-rounded conception of modern plastic surgery.

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ANXIETY IN PREGNANCY AND CHILDBIRTH. By Henriette R. Klein, M.D., Associate in Psychiatry, Columbia College of Physicians and Surgeons; Howard W. Potter, M.D., Professor of Psychiatry, Long Island College of Medicine; and Ruth B. Dyk, M.S., Research Department, New York City Youth Board. Paul B. Hoeber, Inc., 1950. $2.75.

This slender volume reports the results of interviews with 27 primigravidae (erroneously referred to as primiparae throughout the book) who were attending the public prenatal clinic at the Long Island College Hospital between September 1945 and June 1946. Interviewing was done by a psychiatric social worker. The authors, two psychiatrists and the above-mentioned social worker, wanted to find out why childbearing is a trying experience for some, but easy and enjoyable for others. The patients were asked about attitudes, misconceptions, superstitions, and anxieties. Because the subjects of the study admittedly had almost no intellectual interests, had been exposed to a minimum of formal education, and were not used to verbalizing about themselves, one wonders about the significance of the information obtained from this peculiar sample of the obstetric population. The 12 points brought out in the summary are well known to most obstetricians who have been observant attendants in any large prenatal clinic. Posibly, however, these concepts are not equally familiar to psychiatrists, for whom the volume may have a modest value.

The appendix contains summaries of the histories of the 27 subjects. The book is nicely made but there is no index.

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THE GENEALOGY OF GYNAECOLOGY — History of the Development of Gynaecology Throughout the Ages— 2000 B.C. - 1800 A.D. with excerpts from the many authors who have contributed to the various phases of the subject. By James V. Ricci, A.B., M.D., Clinical Professor of Gynaecology and Obstetrics, New York Medical College. Second Edition. The Blakiston Company, Philadelphia, 1950. $8.50.

The issuance of a second and enlarged edition of Ricci's "Genealogy of Gynaecology" speaks well not only for the book but also for the intellectual state of our profession which, in spite of the uncertainties of the immediate and somewhat nebulous future, still is in the mood to concern itself with the past of medicine. Like other Ricci contributions to the history of obstetrics and gynecology his Genealogy presents a scholarly survey of a huge volume of recorded knowledge beginning with the nebulous past of the second pre-Christian millenium and ending with the close of the 18th century when gynecology was about to emerge from a long and stale impasse. Ricci has succeeded admirably in condensing a monumental mass of information into a readable tome of some 500 pages. He traces the development of gynecologic diagnosis and therapy step by step from the dim past when priests and shamans of the Mediterranean and Far-Eastern worlds were probing into the physiology of the female genital organs, but only to founder in a sea of superstitions, to the dawn of gynecology when John Hunter said in 1785 that he saw no reason why a woman should not suffer spaying without danger as well as other animals do, and that merely making an opening into the abdomen was not highly dangerous. Every page of this treatise is replete with the type of information that stimulates thought and makes the reader pause in wonderment over man's ever-present fallibility.

In writing the development of gynecology Ricci follows the accepted epochal divisions of the history of medicine. Where the past is vague and confused the author contents himself with merely citing the fragmentary bits of information which have come down to us on papyri and clay tablets. Where the knowledge of the past was preserved through word of mouth but not recorded until centuries later he has aimed to clarify obscure issues by comparing the several versions of the recorders. The later knowledge as recorded by the printing press he has sifted and correlated to make a readable whole. As in other publications Ricci presents a wealth of detailed annotations and reliable source of references. The material is presented in an orderly fashion yet it is not of the stuff that makes for casual reading. However, for the discriminating reader and in particular for the student of history, regardless whether medical or otherwise, Ricci's treatise will prove itself invaluable aside from making delightful reading.

Dr. Edward A. Schumann of Philadelphia, author of outstanding contributions to gynecology and obstetrics, has written a sparkling introduction for the second edition. The Blakiston Company has seen to it that the printing (The Maple Press Company of York, Pa.), the paper and the binding are of the highest quality, yet the cost has been held down to $8.50, a bargain in view of the high cost of printing and binding. Your reviewer considers the second edition of Ricci's "Genealogy of Gynaecology" an outstanding contribution to the history of medicine and a valuable reference book.

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CLINICAL ELECTROCARDIOGRAPHY. By Francis F. Rosenbaum, M.D., Assistant Clinical Professor of Medicine, Marquette University School of Medicine. Edited by Henry A. Christian, A.M., M.D., LL.D., Sc.D., Hersey Professor of the Theory and Practice of Physic, Emeritus, Harvard University. Oxford University Press, New York, 1950. $4.50.

This concise monograph on the electrocardiogram is among the best of recent texts on this subject. The author, well qualified to speak for the Wilson school of electrocardiographic interpretation, does so in lucid, well organized sections.

The electrocardiographic reproductions are excellent and are conveniently arranged with the text and with pertinent facts of illustrative case histories. The emphasis placed upon the limitations of the electrocardiogram and its proper use in clinical medicine gives the book unique value as an introduction for the beginner, and as a reminder to the over-enthusiastic electrocardiographic interpreter.

One minor annoyance in the book is the retention of the same page numbers as in the original Oxford Loose Leaf Medicine from which this monograph was reprinted. Otherwise the make-up of the book, its index and bibliographic arrangement are entirely adequate.

This book deserves a place in the library of every physician interested in cardiovascular disease, and can be read with profit by all who are interested in the clinical application of the electrocardiogram.

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DISEASES OF THE HEART. By Charles K. Friedberg, M.D., Associate Physician, Mount Sinai Hospital, New York. W. B. Saunders Company, Philadelphia, 1949. $11.50.

The author presents this book as an effort "to provide a comprehensive and integrated exposition of the diseases of the heart." In the reviewer's opinion the book fulfills this purpose and is the best of the more recent books on cardiac disease. Its method of presentation presupposes some fundamental information on the part of the reader in cardiovascular physiology and electrocardiography, so that it should prove more helpful as a reference text for the advanced student than as an introduction for the beginner in the study of heart disease.

The organization of the material presented is excellent and the various sections are conveniently divided into chapters which make for ease in reading and reference. The subject matter is more complete and current than any other available text in this field, and opposing views of controversial questions are adequately summarized.

The section on circulatory failure is an outstanding one and should be read by every internist who has been unable to keep abreast of the voluminous literature related to this problem in recent years.

Unfortunately, titles are not included with the references. Because of that space-saving device the greatest value of a remarkably complete bibliography cannot be attained. Revision of the bibliography in succeeding editions with this in view would add greatly to the book as a reference work.

TEXTBOOK OF ENDOCRINOLOGY. Edited by Robert H. Williams, M.D., Executive Officer and Professor of Medicine, University of Washington Medical School, Seattle. W. B. Saunders Company, Philadelphia, 1950. $10.00.

During the past three decades many of the hormones have been made available in pure form and much has been learned of the manner in which they influence propagation, growth, maturation and general metabolic activities. With the accumulation of such knowledge there has been acquired a much better understanding of the clinical endocrinopathies. This book discusses the management of these conditions based on the application of fundamental information. It fills a long-felt need for an authoritative text on clinical endocrinology.

The editor himself has written chapters on the general principles of endocrinology, the laboratory procedures involved, the pituitary gland and the thyroid gland. He has had the collaboration of experienced investigators and teachers in the remaining chapters. The headings of the chapters and their authors include: Chronic Adrenal Hyperfunction (Edwin J. Kepler and William Locke), Adrenal Cortical Insufficiency and the Pancreas and Diabetes Mellitus (George W. Thorn and Peter H. Forshan), The Testes (John Eager Howard and William Wallace Scott), the Ovaries (George Van S. Smith), Diseases of the Parathyroid Glands (Edward C. Reifenstein, Jr.), Influence of Endocrine Glands Upon Growth and Development (Lawson Wilkins), Neuroendocrine and Psychodynamic Aspects of the Endocrinopathies (Harry B. Friedgood) and Obesity (L. H. Newburgh).

The subjects are discussed with clarity and brevity enough for the book to be used as a text in medical schools. There is also sufficient detail for it to serve as a reference for the student or physician. The photographs are good, except for some of those reproduced from the older medical literature. The volume is a welcome addition to the literature of internal medicine.

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DISEASES OF THE FOOT. By Emil D. W. Hauser, M.S., M.D., Associate Professor of Bone and Joint Surgery, Northwestern University Medical School. Second Edition. W. B. Saunders Company, Philadelphia, 1950. $7.00.

This second edition of "Diseases of the Foot" covers the anatomy, the physiology, the diagnosis and the treatment of the many abnormal conditions found, rarely as well as frequently, in the feet. Many excellently reproduced roentgenograms, photographs and line drawings are valuable in illustrating the details of pathologic conditions of the foot. For instance, the accessory bones of the foot are covered in a way that will aid the specialist, as well as the general practitioner, in differentiating normal findings that are often mistaken for abnormal, and vice versa.

The orthopedic specialist will find the book valuable, because it represents the considered views of a careful man who has spent the major part of a professional life in the study of feet, of gait and of posture. The author probably expects the specialist to disagree with certain of his ideas about indications for therapy and the way the therapy is carried out. At the same time, the specialist will benefit by reviewing his own reasons for his favored forms of therapy and his reasons for differing with the author. Many in this country follow Hiram Kite of Atlanta in the therapy of club feet and it is probable that the novice can more easily follow Kite than Hauser. An inexperienced man would probably run into difficulty in trying to follow Hauser in the correction of a deformed foot by using the Thomas wrench. In Hauser's hands it is probably useful.

The diagnostician and the general practitioner will find the book valuable for reference but the general man will likely have difficulty in following certain of the detailed instructions.